FOOD AND DRUG ADMINISTRATION

CENTER FOR TOBACCO PRODUCTS

TOBACCO PRODUCTS SCIENTIFIC ADVISORY COMMITTEE MEETING

MARCH 31, 2010

NTSB CONFERENCE CENTER

429 L'ENFANT PLAZA

WASHINGTON, D.C.

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Ex Officio Members:

URSULA BAUER, Ph.D.

H. WESTLEY CLARK, M.D.

SUSAN V. KAROL, M.D.

FDA Participants:

LAWRENCE DEYTON, M.D.

CORINNE G. HUSTEN, M.D.

C O N T E N T S

ITEM:

P R O C E E D I N G S

DR. SAMET: Good morning. We're going to go ahead and get started.

I'm John Samet, the Chair of the Tobacco Products Scientific Advisory Committee, aka TPSAC. Thank you for being here and joining us.

I need to make a few statements as we get started. For topics, such as those being discussed at today's meetings, their often are a variety of opinions, some of which are quite strongly held. Our goal at today's meeting will be a fair and open forum for discussion of these issues, and that individuals can express their views without interruption.

Thus, as a general reminder, individuals will be allowed to speak into the record only if recognized by the Chair. We look forward to a productive meeting.

In the spirit of the Federal Advisory Committee Act, and the Government and the Sunshine Act, we ask that the Advisory Committee members take care that their conversations about the topic at

hand take place in the open forum of the meeting.

We are aware that members of the media are anxious to speak with FDA about these proceedings; however, FDA will refrain from discussing the details of this meeting with the media until its conclusion.

Also, the Committee is reminded to, please, refrain from discussing the meeting topic during breaks or lunch. Thank you.

I would also note that we will have an introduction of the Committee, and some other matters before we move on to the -- to hear from the public. Our complete hour is not yet filled for public comments. If there are additional people here who do want to make comments, there is a sign up sheet outside.

Your comments will be limited to two minutes, as we have a rather full agenda. And should we not in the end after asking questions of those who have already been signed up to speak -- not have time, I'm afraid we will not be able to allow you to speak. In the event of time -- we are

close to schedule, there should be time for some additional public commenters, so you will need to sign up outside.

Let me ask, let's see, that the Committee members and those around the table introduce themselves. Let's start with Dr. Clark.

DR. CLARK: I'm Dr. Westley Clark. I am from the Substance Abuse and Mental Health Services Administration where I am the Director of the Center of Substance Abuse Treatment.

DR. KAROL: Good morning. I am Susan Karol, the Chief Medical Officer for the Indian Health Service.

DR. BAUER: Good morning. I am Ursula Bauer, Director at the National Center for Chronic Disease Prevention and Health Promotion at the Centers for Disease Control and Prevention.

DR. HECK: Hi, I'm Dan Heck, a principal scientist at the Lorillard Tobacco Company, and I'm here representing the tobacco manufacturers.

DR. LAUTERBACH: I'm John Lauterbach. I'm the owner of the Lauterbach & Associates in Macon,

Georgia. We're consultants in tobacco science, chemistry and toxicology of tobacco products. And I'm here representing the small business tobacco manufacturers.

MR. HAMM: I'm Arnold Hamm. I'm the tobacco growers representative.

DR. BENOWITZ: Neal Benowitz, Professor of Medicine. I'm Chief of Clinical Pharmacology, University of California, San Francisco.

MS. DeLEEUW: My name is Karen DeLeeuw. I'm with the Center for Healthy Living at the Colorado Department of Public Health; and I'm a representative of state government.

MS. STARK: I am Cristi Stark. I am the acting Designated Federal Official.

DR. CLANTON: I'm Dr. Mark Clanton. I'm a Pediatrician and Chief Medical Officer of the High Plains Division of the American Cancer Society.

DR. HATSUKAMI: I'm Dorothy Hatsukami from the University of Minnesota, Professor of Psychiatry.

DR. WAKEFIELD: Good morning. I'm Melanie

Wakefield. I'm Director of the Center for Behavioural Research in cancer, at The Cancer Council Victoria in Melbourne Australia.

DR. HENNINGFIELD: Good morning. I'm Jack Henningfield. I am -- research in health policy at Pinney Associates, and I am Professor of Psychiatry and Behavioral Sciences at the John Hopkins University School of Medicine.

DR. NEZ HENDERSON: Good morning. My name is Patricia Nez Henderson. I am the Vice President of the Black Hills Center for American Indian Health.

DR. CONNOLLY: Good morning. My name is Gregory Connolly. I am professor at the Harvard School of Public Health.

DR. HUSTEN: I'm Corinne Husten. I'm senior medical advisor at the Center for Tobacco Products at FDA.

DR. DEYTON: Good morning. I am Lawrence Deyton, Director of the Center for Tobacco Products at FDA.

MS. STARK: Okay. I will now read the

meeting statement. The Food and Drug Administration, FDA, is convening today's meeting of the Tobacco Products Scientific Advisory Committee under the authority of the Federal Advisory Committee Act, FACA, of 1972. With the exception of industry representatives, all members, temporary voting members, temporary nonvoting members, and the guest speakers are special government employees, SGEs, or regular federal employees from other agencies and are subject to Federal conflict of interest laws and regulations.

The following information on the status of this Committee's compliance with Federal ethics and conflict of interest laws covered by, but not limited to, those found at 18 U.S.C Section 208 and Section 712 of the Federal Food, Drug and Cosmetics Act, FD & C Act, is being provided to participants in today's meeting and to the public.

FDA has determined that members and temporary voting members of these committees are in compliance with Federal ethics and conflict of interest laws.

Under 18 U.S.C. Section 208, Congress has authorized FDA to grant waivers to special government employees and regular federal employees who have potential financial conflicts when it's determined that the Agency's need for particular individual services outweighs his or her potential financial conflict of interest.

Under section 712 of the FD & C Act, Congress has authorized FDA to grant waivers to special government employees and regular government employees with potential financial conflict when necessary to afford the Committee essential expertise.

Related to the discussion of today's meeting, members and temporary voting members of this Committee have been screened for potential financial conflicts of interests of their own, as well as those imputed to them, including those of their spouse's or minor children; and for purposes of 18 U.S.C. Section 208, their employer's. These interests may include investments, consulting, expert witness testimony, contracts, grants, gratis,

teaching, speaking, writing, patents and royalties, and primary employment.

Today's agenda involves, one, receiving presentations on the background and overview of the FDA Center for Tobacco Products, the Family Smoking Prevention and Tobacco Control Act, the tobacco control Act, and the Tobacco Products Scientific Advisory Committee.

Two, receiving presentations on and discussing the published literature on menthol as it relates to the demographics of users; preferential use by persons initiating tobacco use; the health effects of menthol in cigarettes; the effects of menthol on addiction and cessation; marketing and consumer perceptions about menthol cigarettes; the sensory qualities of menthol cigarettes; and the effects of menthol and how cigarettes are smoked.

And three, receiving preliminary information about topics that will be discussed at future meetings, including the establishment of a list of harmful and potentially harmful tobacco product constituents, including smoke constituents.

These discussions are preliminary to the preparation of the Tobacco Products Scientific Advisory Committee's required report to the Secretary of Health and Human Services regarding the impact of use of menthol in cigarettes on the public's health.

This is a particular matters meeting during which general issues will be discussed. Based on the agenda for today's meeting and all financial interest reported by the Committee members and temporary voting members, no conflict of interest waivers have been issued in connected with this meeting.

To ensure transparency, we encourage all Standing Committee members and temporary voting members to disclose any public statements that they have made concerning the issues before the Committee.

With respect to FDA's invited industry representatives, we would like to disclose that Drs. Daniel Heck and John Lauterbach, Mr. Luby Hamm are participating in this meeting as non-voting

industry representatives, acting on behalf of the interests of the tobacco manufacturing industry, the small business tobacco manufacturing industry, and tobacco growers respectively. Their role at this meeting is to represent these industries in general and not any particular company.

Dr. Heck is employed by Lorillard Tobacco Company. Dr. Lauterbach is employed by Lauterbach & Associates, LLC; and Mr. Hamm is retired.

FDA encourages all the participants to advise the Committee of any financial relationships that they may have with any firms at issue. Thank you.

In addition, I actually have a request. NTSB would like all members to keep their drinks out of the main board room. We have already had a spill. We would like to prevent future spills.

Also, I would like to remind everyone present to, please, silence their cell phones if they have not already done so. And I would like to identify the FDA press contact. Yesterday, you met Kathleen Quinn, who is one of our contacts. A

second contact is April Bruback (phonetic).

April, if you are here present, please stand. Thank you.

DR. SAMET: Okay. Thank you, Cristi.

Let me just sort of alert everyone to what the agenda looks like for the morning as we get started. I'm just going to give a quick recap of yesterday to remind everyone about what we heard, and what some of the key points are. We then have time for any further clarifying questions from the Committee with regard to yesterday's presentations.

Then, what we will do is move to the public comments. So those of you who are here to make comments, I'm just sort of giving you a warning it may be prior to 9:30 when we get started. Then after the public presentations we will move on to the -- the four questions that we have. I think that order makes sense.

Let me just give a quick summary of what was a very busy day yesterday. We really heard a lot of information, and were presented with some very detailed reviews by our presenters. Certainly,

we began, I think, with a -- an important set of statements by Drs. Koh and Hamburg about the importance of our work for public health.

I think both very eloquently stated how the work of the new center and this Committee will figure in making some very important judgments on the best way to proceed with the -- with the Center's work. The -- our charge was given to us, I think, both in general and specifically around the menthol report; and I think we -- as we begin our activities may want just to look at that again to refresh our memories, and have those words in front of us.

Just, again, a reminder of what we heard yesterday. We heard summaries of -- largely of the published literature with some additional new analyses of data on use presented by Ralph Caraballo from the CDC. I will have to mention I heard at least five different pronunciations of his name yesterday.

So we heard summaries. And again, those were -- much of that was based on the systematic

review of the literature that had been done originally by the National Cancer Institute, but then had been updated. From Dr. Caraballo we heard about variation in use of mentholated cigarettes by people by racial and ethnic group, and also over time. I think his presentation made clear that use patterns are very -- they have been heterogenous by a group in our country for a substantial period of time; but there are also time changes in use patterns of these products.

Dr. Lawrence told us about the studies that have been published on the smoking topography and the sensory effects of menthol, describing a somewhat variable picture in looking at the -- the studies of smoking topography. And again, she commented on the relatively small number of studies, and the somewhat variable findings. And then, again, reviewed the sensory effects.

We heard about consumer perceptions of these products; and I think learned that there was a clear differentiation, in general, of the menthol products from the nonmenthol products. And that

there were certain consumer perceptions of them that were relatively firmly identified.

In three presentations we heard about the consequences of the -- the availability of menthol cigarettes in relationship to initiation, starting to smoke, dependence, and cessation.

Again, here we heard -- we heard about a variety of studies conducted over time. Some of them having limitations potentially of size; and again, presenting a picture of what evidence was available. And I think giving us some ideas of what additional evidence we may want to seek to better understand menthol cigarettes, and initiation, dependence, and cessation, obviously, critical for public health.

And we heard about some of the challenges, I think, of trying to understand the role of race, ethnicity, genetics, perception and menthol as they are sort of intertwined in this literature.

Then, finally, in the last presentation from Dr. Hoffman, we heard about studies of health risks; and that is whether there were studies

specifically speaking to the question of whether risks for the well-known health consequences of smoking were different, to a meaning extent, to people using menthol cigarettes versus those using nonmenthol cigarettes.

So that's a very quick summary of an awful lot of slides. And again, we have access to those materials, slides; and of course, we were provided with the bibliography in advance of the meeting.

So I think just with that quick recap, what I suggest we do is we take whatever time now -- I guess all our speakers from yesterday are here. Perhaps Dr. Caraballo is not. But -- oh, he is here.

Okay. If there are questions -- clarifying questions in relationship to those presentations. John.

DR. LAUTERBACH: On the demographics of menthol use, and we were finishing up yesterday dealing with potential health effects of menthol. Is the use of menthol cigarettes across the country uniform, or are they more prevalent, say, in rural

areas or urban areas?

DR. SAMET: Let's see. I think, Ralph, do you want to come on up.

DR. CARABALLO: So the question is, if there is differences by region, rural areas, urban areas of menthol use?

I came across with the bibliography of one study that looked at it by region -- in fact, I think it was the Gary Giovino study included some analysis by region. And definitely, yes, there are differences by region. He didn't look at urban versus rural, but we know that African Americans in the United States, which is a group that consume more menthol cigarettes among their smokers, are concentrated in certain areas of the United States. Many in the south and the northeast, et cetera. So, yes, there is going to be more concentration of menthol cigarette use in certain parts of the United States.

DR. SAMET: Actually, before you go away, as a further question; if we did want additional analyses of the survey data you presented to better

understand regional differences, at least broadly, urban, rural; you might be able to carry out such analyses?

DR. CARABALLO: Yes, I think Dr. Giovino looked at NSDUH when he looked for it by region; so I believe, yeah, it will be possible. You are right.

DR. SAMET: Okay. Thank you. Dan.

DR. HECK: Just a comment to some of the later discussion today, yesterday --

DR. SAMET: Is that a comment or question?

DR. HECK: I guess it was more of a comment I wanted to offer.

Having recently reviewed the vast literature on menthol myself recently, I can appreciate the magnitude of the task that staff has in trying to pull together this literature.

I would encourage them, though, to be particularly deliberate and inclusive and comprehensive in their treatment of the biomarkers and the epidemiology data. Because I know, as Jack reminded us yesterday a few times, the principal

dose and response is important here. And the biomarkers data that we have available are probably the best approximation of the differences in dose or exposure that may -- may or may not accompany menthol cigarettes.

And the disease epidemiology is, I think, the closest indicator we have, the most meaningful indicator of the ultimate outcome of many differences that may exist. That is, differences in chronic disease risk. So those areas, I think, need to be particularly deliberately covered in their entirety in the distilled fashion for the consideration by the Committee.

DR. SAMET: Okay. Thank you. I think when we return to our discussion of the questions, I think this will be a topic to turn to.

Okay. Let's see, other clarifying questions from the Committee?

Okay. Then we are going to move on to the public -- to open public hearing. Again, I have some materials I need to read to you.

Both the Food and Drug Administration, the

FDA, and the public believe in the transparent process for information gathering and decision making. To ensure such transparency at the open public hearing session Advisory Panel meeting, FDA believes that it is important to understand the context of an individual's presentation. For this reason, the FDA encourages you, the open public hearing speaker, at the beginning of your written or oral statement to advise the Committee of any financial relationship that you may have with a sponsor, its product, and if known, its direct competitors.

For example, this financial information may include the sponsor's payment of your travel, lodging, or other expenses in connection with your attendance at the meeting.

Likewise, FDA encourages you at the beginning of your statement to advise the Committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking.

The FDA and this Committee place great importance in the open public hearing process. The insights and comments provided can help the Agency and this Committee in their consideration of the issues before them.

That said, in many instances and for many topics there will be a variety of opinions. One of our goals today is for this open public hearing to be conducted in a fair and open way where every participant is listened to carefully, and treated with dignity, courtesy, and respect. Therefore, speak only when recognized by the Chair, and thank you for your cooperation.

Now, I would also note for the Committee members that after the presentations we can ask clarifying questions. Remember that we have limited time, so these should be targeted clarifying questions, but we do have time.

And again, for the speakers, I believe that you have all been allotted time slots -- is anyone aware of their individual spots?

I think some of the groups have eight

minutes. You will get a warning. You will get a one minute warning. When you are done, you are done. So, please, adhere to the time. And if we are ready, our first public presenter is Katharine Swartz.

MS. SWARTZ: Good morning. My name is Katharine Swartz. And I'm a Masters in Public Health Candidate at the Keck School of Medicine at the University of Southern California. The Preventative Medicine Department at the Keck School of Medicine at USC is funding my trip here today.

The continued addition of menthol to cigarettes directly undermines the intention of the Family Smoking Prevention and Tobacco Control Act, which is to prevent youth from using tobacco.

I propose that menthol should be banned completely from cigarettes and their components parts, and the flavor restrictions of Section 907(A)(1)(a) for the following three reasons.

The first reason menthol should be banned in the flavor clause is because regardless of its addictive qualities, menthol is added to cigarettes

to change the taste.

Secondly, menthol should be banned because it masks the harshness of cigarettes smoke.

Finally, menthol should be banned from cigarettes because its ability to enhance taste and mask harshness facilitates youth uptake of smoking and increases the addictive potential of cigarettes.

To begin, the precedence of menthol's inclusion in the flavor ban in HR 1256 is based on restrictions of candy flavor, such as coconut and pineapple in cigarettes or their component parts. These ingredients and many more are banned because of their appeal to youth in both flavor and advertising, not because they are additive.

The scientific community has not found that flavors, such as coconut or pineapple make people smoke more. Although menthol is a different kind of flavoring agent, it is a flavoring agent nonetheless.

Like other flavors menthol stimulates the taste buds, in addition to its unique stimulation of cold receptors in the mouth and nose, leaving

smokers with a minty cooling sensation. Among children, menthol is a flavor associated with peppermint candy, chewing gum, and toothpaste. If children consider it a flavor, so should the FDA, which brings me to my second point.

Menthol doesn't just change the taste of cigarettes. Menthol masks the harshness of cigarette smoke, making it easier to inhale. In the 2006 study by Hersey, et al. new and younger smokers preferred mentholated cigarettes because of diminished sensations of harshness and discomfort upon inhalation. This is due to menthol's anesthetic characteristics, which even in low concentrations suits the respiratory tract and the coarseness of cigarette smoke.

It is through the elimination of these negative physiological reactions that menthol facilitates youth uptake, which leads to my final point.

Even in its smallest concentrations cooling menthol smooths over hacking and coughing allowing you to smoke cigarettes with less physical

irritation. It is because of these taste enhancing and masking characteristics that mentholated cigarettes have achieved status as a popular beginner cigarettes among American youth.

The fewer physiological reactions a person has to smoking, the more likely it is that they will continue smoking in the future. It is also more likely that they will become addicted. This is the additional health risk posed by cigarettes that contain menthol.

In a 1998 description of the concessions back then Phillip Morris would make in a FDA Bill, Mark Berlin cited a fear that the government would require them to add ingredients to make cigarettes taste worse. So why would the FDA permit an ingredient that make cigarettes taste better?

In conclusion, the purpose of the flavor band in HR 1256 was to decrease the appeal of cigarettes to children. In high concentrations menthol has a strong cooling minty flavor. In low concentrations menthol covers harsh cigarette smoke. Menthol's ability to change the taste and mask the

harshness of cigarette smoke enhances its addictive potential, putting our children's future at risk. Menthol should be considered because it is a flavor, and all other flavors have been banned.

For these reasons and for the protection of our children, it is essential that the FDA take action by banning menthol from inclusion in cigarettes for any of their component parts today. Thank you.

DR. SAMET: Okay. Thank you. And are there clarifying questions? John.

DR. LAUTERBACH: On the subject of menthol and harshness, do you have trained sensory panel data to support your conclusions, or are you just going by statements that were taken from tobacco documents? Also, if you have considered any other factors affecting harshness, such as tobacco moisture, or even things in no additive products that can make the cigarette very harsh.

MS. SWARTZ: I am aware that cigarettes that contain menthol have received higher ratings of lower harshness by youth than other cigarettes, but

I don't have something I can cite directly right now.

DR. SAMET: Other. Mark.

DR. CLANTON: Our Panel got an extensive review of the literature when it comes to physical and perceived effects of menthol yesterday. So we're familiar with most of the information you provided.

We also talked a little bit about marketing. So I'm going to ask you a question that goes -- it's almost an a priori question. So when a child or an adolescent takes the first puff of a menthol cigarette we know what happens. How do you think the kids get to those first puffs? In other words, what do you think about the strategies that lead kids to menthol cigarettes, as opposed to other cigarettes?

Is there some sort of communication network or marketing or something that brings them to those physical and physiologic effects?

MS. SWARTZ: That's a very interesting question.

Menthol, unlike a lot of different flavors, hasn't been advertised as a candy cigarette, because it isn't necessarily a candy flavor. However, there is a lot of advertising in -- you were asking about different networks. You Tube has several different advertisements on it for menthol.

So for instance, if you search Marlboro menthol cigarettes, it is very easy to find an advisement that was done by a musical event. So it has this beautiful graphic image of menthol -- menthol cigarettes, and the green and the minty; and then it has a DJ making music underneath a green menthol banner in the shape of Marlboro's unique logo.

DR. SAMET: Okay. Greg.

DR. CONNOLLY: I was just intrigued by your statement that maybe there should be a counter -- I mean, a counter constituent added that alerts the consumer to the toxicity of the product, rather than, as you have asserted, masks the potential toxicity. I was really intrigued by that.

Do you think rather than taking menthol out, that one should consider adding something like SBI to natural gas to alert the consumer of the toxicity?

MS. SWARTZ: That's an excellent idea. In fact, in the same 1998 document from Phillip Morris, they cited that they were concerned that the FDA would add something to make it taste worse. So there are actually different ingredients that you can add to make cigarettes taste worse. I believe that in the interest of the public health that our Committee should do something that could make them taste worse; but removing menthol helps. Menthol addition is meant to cover the naturally distasteful flavor that children are probably not inclined to have in their mouth.

DR. SAMET: Dan.

DR. HECK: Let's recall that about 70 percent -- about 70 percent of smokers don't prefer menthol, or actively dislike it, or for whatever reason do not choose menthol. I think a blanket assertion that menthol is invariably more

appealing to one group or another has to be examined carefully. Certainly, not to smokers overall. If you have a comment on that.

MS. SWARTZ: The question here is not necessarily if it's more distasteful to adults, but rather to children. So children are probably less likely to continue inhaling something that is harsh on their throats or in their mouths. People -- 70 percent of smokers aren't children. So we can say that the first puff is probably contingent upon the taste for the cigarettes, an interest in continuing inhaling.

DR. SAMET: Okay. Thank you. I think we need to move on. Thank you, Katharine.

Our next speaker is Mr. William R. True from Lorillard Tobacco Company. Mr. True.

DR. TRUE: Good morning. We thank the Committee for the opportunity to share these brief comments. The answer to the overarching question before this Committee is, menthol does not make cigarettes more harmful; and the science supporting this conclusion is clear and compelling.

Menthol has been used safely in food, drink, and cosmetic for decades. Menthol in cigarettes is delivered largely unchanged in the smoke without any meaningful effects on smoke chemistry and toxicity. The impact on menthol cigarettes on public health must be determined by using the most powerful scientific tool. Those tools that provide direct, measurable outcomes are evaluated with statistical rigor as opposed to subjective surveys and speculation.

We are fortunate that the effects of menthol cigarettes have been extensively studied in human smokers, including at least a dozen epidemiology studies, and several large exposure biomarker studies. As a result, the evidence on menthol can be considered on an integrated basis, the idea approach to draw sound scientific conclusions.

For decades epidemiology has been the cornerstone of public health judgments, because public health authorities recognize and it provides the most definitive information about health effects

of smoking.

In contrast, to the selected epidemiology studies and results presented yesterday, a thorough consideration of the full body of epidemiology overwhelmingly shows that menthol cigarettes are no riskier than nonmenthol cigarettes. Likewise, human biomarker studies, including several of the largest ever conducted, conclusively show that the actual exposures are similar for menthol and nonmenthol smokers.

Smoking behaviors, such as depth of inhalation, vary widely among individual smokers of all types of cigarettes. Ultimately, these difficult to measure behaviors are significant only to the extent that they effect the smoker's actual exposure to smoke. The informative biomarker studies on the outcome of smoking and -- answer the key question what is the smoker exposed to, rather than how did the smoker smoke.

So when judged by integrating the most quantitative measures of the outcome of smoking, the clear science-based judgment must be that menthol

cigarettes are not more harmful than nonmenthol cigarettes.

I would like to turn now to the question of whether it may be harder to quit menthol cigarettes. Quitting smoking can be difficult for all smokers. Several large national studies of quitting among thousands of smokers have shown no differences in dependence or cessation for menthol cigarettes. These studies are broadly representative of the total smoking population and reflect a vast majority of smokers who quit without the assistance of cessation clinics.

By contrast, smoking cessation clinic studies are effective in evaluating the success of medication and aids that may assist smokers who find it particularly difficult to quit. Clinic participants commonly indicate that numerous stresses of everyday life, such as unemployment or lower income are powerfully associated with difficulty in quitting. It is simply beyond the capability of any of these studies and study designs to establish that menthol, as an independent

variable, effects smoking cessation or dependence.

Further, the overwhelming weight of epidemiology shows that menthol and nonmenthol cigarettes are the same in terms of disease occurrence across races and sexes, and is strongly consistent with the conclusion that menthol cigarettes are no more difficult to quit.

Finally, I will address the issue of menthol cigarettes and youth smoking. Youth smoking rates have been declining for years, and are now at an all time low. The majority of underage smokers report that the usual brand is not menthol. Surveys report that the top three cigarette brands smoked by adults are also the top three brands smoked by youth, only one of which is a menthol cigarettes.

Given that underaged smokers cannot legally obtain cigarettes, this correlation in reported brands is not surprising. Youth simply smoke what is accessible to them, and that is typically a nonmenthol cigarette. Such surveys, however, were not designed and cannot be used to determine an independent effect of menthol on

decisions of youth to experiment with or continue smoking. When you look at the impact of menthol cigarettes on youth smoking rates, the data show that the use of menthol cigarettes is unrelated to youth smoking rates, and they actually have a slight inverse correlation.

Twenty-one states have a menthol market share that's higher than the national average; of these, 20 have youth smoking rates lower than the national average.

Remarkably, right here in the District of Columbia we see the highest menthol market share in the country, and one of the lowest youth smoking rates. In addition, despite the popularity of menthol cigarettes among African American youth, the facts are compelling. They smoke at about half the rate of white youth, and they start smoking later in life. Based on these measurable outcomes, menthol cigarettes are clearly not associated with higher youth smoking rates. There is no data to indicates that if menthol cigarettes were not available youth smoking rates would change.

I would like to conclude by saying that with respect to public health, using the best methods available to science, a menthol cigarette is, well, just another cigarette, and should be treated no different. Thank you.

DR. SAMET: Okay. Let's see, who would like to -- question.

Let me begin with a first question. I appreciate the submission to the Panel that you made and your comments, which largely refer to the open peer reviewed literature. I think it will be helpful to have an understanding of research that have gone on at Lorillard, and, perhaps, other companies in relationship to determination of the amount of menthol in cigarettes, perception, biomarker studies. Research that's not in the public -- in the public domain, which we can readily identify. We need to be able to view all the evidence.

DR. TRUE: Yes, my understanding is that will be the topic of the next meeting potentially for us to disclose to you and discuss all the

Lorillard specific research.

DR. SAMET: Right. So perhaps, you can give us some insights into the scope of research that has not been available because it's unpublished, and the kinds of laboratory investigation that have been carried out at Lorillard.

DR. TRUE: Well, one of the most significant biomarker studies that was done recently, published by Dr. Heck in 2009, which is part of your public literature. And we continue to look at the overall, you know, effects of our products and our consumer preferences; and we continue to do that work.

DR. SAMET: Okay. Well, thank you. My question was directly in reference to literature that we might not be able to access, because it's not published yet. Again, we will be making that request to understand what's available.

DR. TRUE: Yes, we have addressed many of the topics that have come up over the last couple of days. We have addressed a number of those topics in

various studies. Those are either ready to be published, to be published, or under submission for the next meeting.

DR. SAMET: Okay. Thank you, Greg.

DR. CONNOLLY: It's my understanding that menthol cigarettes comprise 21 percent or greater of the market share in the United States and most recent -- most recent Federal Trade Commission report was 27 percent, the year before 21.

What was the percent of cigarettes that were mentholated 40 years ago? That's my first question.

DR. TRUE: I don't know that.

DR. CONNOLLY: Okay. Second question. Is menthol essential to smoking?

DR. TRUE: I don't believe that menthol is essential to smoking, no.

DR. SAMET: Jack.

DR. HENNINGFIELD: You touched on the issue of whether or not menthol makes cigarettes more harmful. I assume you agree that cigarette smoking is harmful.

DR. TRUE: Cigarette smoking is harmful.

DR. HENNINGFIELD: And so one of the things we're trying to address is menthol -- the nature and seriousness of menthol's potential harm. Would you agree that if people start smoking that's a very harmful behavior?

DR. TRUE: Yes, sir.

DR. HENNINGFIELD: So one of things we need to figure out is the degree to which menthol promotes initiation in people who would not otherwise have begun smoking; and not just in the overall population, but in subpopulations. And for example, if there is a primary concern among African Americans -- and that appears to be the case, but this is something that we have to thoroughly flush out -- then that will be a potential very harmful effect.

And I think what we need to do is evaluate the strength, the evidence for that, and information that you may have on your own studies, tracking studies that could help us understand that better, I think would be very useful; including information on

studies on switching from one brand to another. Because I think another area we need to figure out is to what degree are some people switching from nonmenthol to menthol cigarettes instead of quitting or delaying quitting, because I'm sure you understand that smoking --

DR. SAMET: Not to cut you off. Maybe quick clarifying questions is probably where we should be here.

DR. HENNINGFIELD: Okay. So those kind of data are data --

DR. SAMET: Yes, seems like maybe you are getting at what we might be requesting. If you have a clarifying question for Mr. True's presentation.

DR. HENNINGFIELD: Okay. I guess I was looking for what kinds of data we might be able to get.

DR. TRUE: Dr. Henningfield, I would submit that we look at the actual market share data, which is the actual outcome of what consumers are purchasing in terms of menthol versus nonmenthol. Again, if you look at the states with the highest

menthol market share, we are below average. In some cases significantly below average in youth smoking rates. And the contrary is true in many cases as well. Highest youth smoking states technically are states that are below the average menthol market share.

DR. SAMET: Okay. Karen.

MS. DeLEEUW: Yesterday we heard a little bit of information about the possibility that menthol smokers might be willing to pay more for menthol cigarettes. Do you have any information that would either support or dispute that?

DR. TRUE: No, we haven't studied that directly.

MS. DeLEEUW: Thank you.

DR. SAMET: Okay. Patricia.

DR. NEZ HENDERSON: You stated that African Americans smoke less per day. And my question to you is, in terms of marketing how much do you spend on African American communities versus non-African American communities?

DR. TRUE: Well, first of all, I did not

state they smoke fewer cigarettes per day. I stated that they initiated later, and lower youth smoking rates, and later in life. In terms of our marketing studies, I don't have that information.

DR. SAMET: I think, Dr. Clark.

DR. CLARK: Yes. Thank you for your comment. You addressed adverse impact of menthol; but you, as Dr. Henningfield suggest, didn't address the flip side of that. And the mission of this Committee is to look at the impact of the use of menthol in cigarettes on the public health, which goes beyond, then, the adverse impact. Because as you correctly stated, cigarette smoking is hazardous to your health.

So since this Committee also is suppose to look at the impact on children, African Americans, and Hispanics that creates a -- when you use averaging data, don't you offset the impact on African Americans? Because as we heard yesterday there is a disproportionate use of African Americans. Anything that facilitates use then ultimately facilitates the adverse impact, wouldn't

you agree?

DR. TRUE: I think if you look at the information that was presented yesterday there was a number of information on those studies, and the conclusions of the authors were drawn based on the studies being done. I would say that, you know, there is -- looking at the total population, in fact, is the most reliable way for us today to understand the true impact.

DR. SAMET: Okay. Thank you, Mr. True, for your presentation.

We're going to move on to Brandel France de Bravo, the National Research Center for Women and Families.

MS. FRANCE de BRAVO: Thank you. I am pleased to have the opportunity today to testify on behalf of the National Research Center for Women and Families and its Cancer Prevention and Treatment Fund. I have a Master's in Public Health from Columbia University; and in addition to my position at NRC, I'm an associate at the John Hopkins Bloomberg School of Public Health.

Our Center is dedicated to improving the health and safety of adults and children, and we do that by scrutinizing medical and scientific research to determine what is known and not known about specific treatments and prevention strategies. We do not accept contributions from companies that make medical products or from the tobacco industry.

I should disclose that my mother has stage four lung cancer, but she was never a smoker of menthol cigarettes. Like most smokers, she began smoking as a teenager.

We know from what we heard yesterday that adolescents are more likely to smoke menthol cigarettes than adult smokers. We also know that while smoking is declining among adults and adolescents, menthol cigarettes are becoming more popular among both adults and kids, ages 12 to 17.

Anything that makes smoking more attractive or tolerable in adolescence, whether it's a flavor or the perception that the models in ads for menthol cigarettes are younger and hipper, will only add to our country's burden of addiction and

lung disease, including lung cancer. We know that if kids can get through adolescence without smoking, they stand an excellent chance of never smoking.

Dr. Rising shared with us yesterday these facts, about 90 percent of smokers tired their first cigarette before 18; and about 70 percent were smoking daily by age 18.

We also learned yesterday from Dr. Hoffman that menthol smokers, young and old, appear more dependent on cigarettes by many measures than nonmenthol smokers. Among 2,000 secondary school kids surveyed in 2006, Black youth scored highest on all the measures of dependence, which included number of cigarettes smoked in their lifetime, number of days per month they smoked, shortest time since the last cigarettes, and likelihood of being a daily smoker.

We know that African Americans are more likely to smoke menthol cigarettes than any other racial or ethnic group, and that magazines and billboards targeted to African Americans are far more likely to advertise menthol cigarettes than

nonmenthol cigarettes.

The literature review presented yesterday raised as many questions as it answered. It's clear that more research needs to be carried out, and members of this very Committee have suggested many worthwhile topics. As scientists, we are prime to ask questions and ask that research be done to answer them. As public health experts, however, I think we can agree on a few things without doing any additional research.

Some of our most vulnerable populations, including communities with huge, huge health disparities appear to be most susceptible to menthol's appeal; adolescents, Blacks, Hispanics, and women. And as a result, they will develop lifelong habits that will lead to disease and disability.

As their overall U.S. market declines, cigarette manufacturers have seized on menthol's competitive advantage. Introducing light menthol brands for new and young smokers who prefer that, and stronger menthol cigarettes for the more

experienced and older smokers who crave that. Now that all flavors other than menthol has been banned, menthol has become the industry's last holdout and last hope for disguising the taste of tobacco.

Several studies cited by Dr. Hoffman suggest that part of the problem with menthol is that it masks problems. Smokers of menthol cigarettes may not be able to perceive changes in health as readily. A spoonful of sugar makes the medicine go down, but cigarettes aren't medicine. They are the main cause of lung cancer; the number one cause of cancer deaths, and they are poisonous to our health. We should not allow companies to sweeten the poison.

Industry will try to convince us that the research on the dangers of menthol cigarettes isn't convincing. There will be pressure to study and stall; but I am here today to beg you, don't drink the Kool-Aid. Just because it's cool and refreshing doesn't mean it won't kill you.

We urge you to advise banning menthol cigarettes just as other flavored cigarettes have

been banned. Thank you.

DR. SAMET: Okay. Thank you for your presentation. Are there clarifying questions from the Committee. Greg.

DR. CONNOLLY: I was curious. You seem to segment out the issue of scientific assessment from policy action. That sort of surprises me, you know, being in a school of public health. My question is -- one of the schools of public health -- is it -- don't you view translation of science -- taking science and translating it into public health -- as being a unity and not a separate activity?

MS. FRANCE de BRAVO: Absolutely. Obviously, when one makes public testimony I am trying to persuade. And as you saw yesterday there is a wealth of data, and it's -- a lot of it is conflicting, and it's very, very confusing. I picked out of it what I feel is pretty clear.

You know, every study -- the abstract for every study that's been financed by the industry always ends with the line that menthol does not in

any way epidemiologically show any increased risk of developing cancer, et cetera, et cetera.

I mean, there are ways of cherry picking this data. I just think that there is a common sense that needs to be looked at here. If cigarette sales are down, if smoking is down, and yet menthol is up, there is something going on here that I just wanted to kind of pierce through the numbers look at some of the most salient points of what was presented yesterday. All I did was draw on the research presented yesterday, all of which you all heard. I'm not telling you anything new. I guess what I am trying to do is peel away some of the stuff that may be confusing to you and try to get at the heart of the matter. I am still using --

DR. SAMET: Okay. Let's move on to our next question. Mark.

DR. CLANTON: It's clear that the initiation of smoking among African American youth is different. We have heard that data over and over within the general population or even other subpopulations. I have to ask your opinion if --

not only do African Americans initiate with menthol, but they persist with menthol. What would happen if there were no menthol to African American adoption rates and the smoking rates if menthol were removed completely, in your opinion?

MS. FRANCE de BRAVO: I can't guarantee -- I feel that we're going to see people adopting at least later, which probably means fewer smokers. If the menthol is more appealing to youth in general, and more appealing to African American youth for a variety of reasons, because it's perceived as healthful, perhaps, or just more cooling or easier to take, and because it's marketed to them, I have to believe that not having menthol availability means that at least some percentage of youth are not going to initiate. I can't quantify that, obviously.

DR. SAMET: Dan.

DR. HECK: I do appreciate the speaker's frankness in describing her representation of the literature as selective to attain the public health message she has delivered. But I think this

Committee doesn't have that luxury of selectively looking at the epidemiology or any other topic. We do have the obligation to look at all of that data, and certainly to the extent that the epidemiology speaks to a lack of risk, it is not the tobacco's industry spin. The data is what it is. That's what we have to consider.

MS. FRANCE de BRAVO: May I comment on that?

DR. SAMET: Certainly.

MS. FRANCE de BRAVO: We're not saying -- I'm saying that menthol cigarettes kill faster and better than regular cigarettes. What we're talking about is their appeal, initiation, feelings of dependence, and the targeting of certain communities. That's really what we're getting at here.

DR. HECK: Yeah, I think that -- that topic will be addressed.

DR. SAMET: Okay. I think we are going to move on. Thank you very much for your comments.

Okay. We're moving on to not our fifth

speaker, but our fourth speaker, Dr. Cheryl Healton from Legacy.

DR. HEALTON: Good morning. Thank you for the opportunity to testify today before this very important body. My name is Cheryl Healton. I am President and CEO of Legacy, and Professor of Public Health at Columbia University. My full testimony has been submitted for the record.

Legacy believes that the FDA should prohibit menthol in cigarettes and other tobacco products. Menthol products account for 1/5th of the U.S. market and astonishingly, menthol cigarettes are more of the market share of the flavored cigarettes already prohibited by the Act.

The success of menthol cigarettes is hardly an accident. Literally many hundreds of internal tobacco industry documents conclusively establish that the tobacco industry has for decades systematically developed and marketed menthol products to attract and keep as long term customers millions of starter and youth smokers, racial/ethnic minorities, and African Americans in particular, and

smokers seeking health reassurances.

There are, of course, many unanswered questions surrounding the properties and health effects of menthol cigarettes. Today, I would like to focus on what we already know about menthol cigarettes. What we do know now provides ample reason for the FDA to eliminate menthol in tobacco products. I would submit that the frame work they should be using is what if we were talking about chocolate? Would we be having a protracted debate about whether more people who smoke chocolate flavored cigarettes live longer or not? It is irrelevant.

First, menthol cigarettes serve as a starter product for America's youth, luring them into taking up a deadly addictive habit, which, based on current data, will cause a third to die prematurely of tobacco-related disease, and millions more to become disabled.

Second, menthols have historically been a key part of the tobacco industry's fraudulent health reassurance claim. This campaign, as you know, has

recently been called out by the federal courts.

Third, menthol has been targeted to communities of color, which often bear a disproportionate burden of tobacco-related disease. In fact, approximately, 83 percent of African American smokers smoke menthol.

For my remaining time I would like to elaborate on menthol's impact on youth. Menthols are starter products for new and younger smokers. It doesn't take a rocket scientist -- and I think you all are -- to figure out if you want to get young people to smoke, you give them a cigarette that taste like candy, like a mint; which is, after all, what menthol is, a compound extracted from the peppermint plant.

It also helps if you mask the harsh effects of tobacco smoke with a cooling sensation the way menthol does. Brown and Williamson put it this way in 1987, menthol brands have been said to be a good starter product, because new smokers appear to know that menthol covers up some of the tobacco taste. They already know what the menthol

taste like vis a vie candy.

So we have a cigarette that taste like candy and it is easier on the throat. And guess what, young smokers smoke more menthols than adults do. In fact, while less than a third of smokers over the age of 35 smoke menthol, over 44 percent of smokers, age 12 to 17 do, and the trend appears to be up.

The executive who famously wrote the base of our business is the high school student was talking about Newports, the number one selling menthol brand made by Lorillard. Newports along with other menthol brands have been advertised in publications with substantial youth readership, including "Sports Illustrated," "Spin" and "Sporting News."

RJR's newest brand is teal colored and marketed as light and lushes brand, which is no longer appearing in women's magazines due to the concerted effort of many people -- managed to attract 9.3 percent of adolescent girls in a one year period to describe a Camel as their favorite

brand. We know that 50 percent of these girls, now that they have a favorite brand -- these girls will be 53 percent more likely to go on to smoke, now that they have a favorite brand. There was no similar change in the affinity for Camel among boys in this longitudinal study, which is out online and will be out in Pediatrics in April.

The fact that the tobacco industry has used menthols to lure young people who are diving head first into a potentially life-long addiction is reason alone to prohibit them. The tobacco industry reaps 19.6 billion every year in sales. And as I mentioned, menthols are responsible for approximately 1/5th of the industry sales. They are a growing share of a shrinking market.

Congress did ban a wide array of other flavors. You know which ones they are, cocoa, chocolate, coffee; and as I pointed out earlier, that should be a key issue with respect to menthol.

A number of leading public health organizations have asked you to take up this topic and urged you to eliminate menthol. Former

Secretary Califano and Dr. Luis Sullivan, along with colleagues, called on Congress to act before this Bill was passed. There has been great speculation about why menthol was not in the original Bill. It is now in your hands, and you have the ability to act.

These minty, less irritating cigarettes that lure our kids into a deadly addiction provide the impetus for you to act now. If we can prevent these people from being included as replacement smokers, we have a chance of eradicating an epidemic that kills nearly a half million Americans each year. Thank you for your time.

DR. SAMET: Thank you for your comments. Questions? I see Greg.

DR. CONNOLLY: Dr. Healton, the Legacy Foundation has been very helpful to the scientific community in looking at the internal industry documents made available by the MSA. And over the past day I have become more confused about this issue. I really don't know what the answer is unless we get more data.

Could we expect as a Committee your expertise, help as a foundation in dealing with these documents and informing both the Committee and the FDA?

DR. HEALTON: Certainly, we're happy to help. As I think you know we provided a substantial endowment to UCFS so that they could have the documents not only there and archived appropriately and searchable, but add to the collection. That was pursuant to a requirement within the Master Settlement Agreement; a requirement that actually fell to the National Association of Attorney's Generals. We agreed to take on that obligation so that it would happen in a timely fashion.

So certainly, I'm certain they're willing to help you; and, of course, we are as well.

DR. SAMET: Other questions? Jack.

DR. HENNINGFIELD: One of the challenges in not only figuring out what is happening, but what to do about it is disentangling the product design and engineer from its marketing; and you gave a good example. You have got the product that you showed

where menthol is part of it, but it's also part of the marketing approach. Can you envision a way of removing one of those variables and not addressing the problem?

If the problem is both the menthol as a characterizing flavor and the marketing that goes along with it, is it possible to remove one of those factors? And for example, under the -- with the powers that FDA would have, and subject to the Tobacco Control Act, is it possible to remove marketing to the degree that that would not be a factor?

DR. HEALTON: Can I clarify what your question is. Are you asking could that be done in the context of the study, or could it be done in the context of a regulatory --

DR. HENNINGFIELD: Well, you have done a lot to look at marketing end product. So your organization has really tried to disentangle. I'm not sure how we disentangle the product from how its marketed.

DR. HEALTON: I think it's possible that

that may not be directly relevant. I know it may seem very relevant, given all that you heard yesterday; but there is no question that the 13 plus billion dollars a year that the tobacco industry spends to promote it's, you know, broad array of products works or they wouldn't be doing it. That's why they would choose to spend that kind of money.

By the same token, there is a lot in the tobacco industry documents about concerns about capturing the African American market, and that there may be something that needed to be in the pitch. If you look at the documents, you see that menthol, because of its associated with health products, was made part of the pitch, because it was believed that the inherent qualities of menthol would boost the initiation and -- mainly the initiation and taking up of the habit to begin with. There is a lot of that in the document. So I mean, I think they tell a very specific factual story.

DR. SAMET: Okay. Good. Thank you. I think we need to move on to our next presentation. Thank you, Dr. Healton.

Next, Dr. Pamela Clark from the School of Public Health, University of Maryland; I guess along with Phillip Gardiner from the University of California sharing time.

MS. CLARK: Yes, we are twins.

We want to talk about the case against menthol from the viewpoint of the -- how do we change this -- the viewpoint of a conference that was held recently; and we want you to keep two things in mind as we talk. One is, we absolutely need to broaden our definition of harm. Our harm cannot be just toxicological harm, and say we have done our job. The other thing is it's time to take the handle off the pump.

When Dr. Snow took the handle off the pump, he had not identified the organisms responsible for the problem. He just did the logical thing based upon the evidence that was already there and took the handle off the pump.

143 tobacco control scientists and front line tobacco control practitioners came together in October of 2009. This was a follow on to a

conference in 2002 that resulted in a very landmark issue of nicotine and tobacco research that has been floated again, and again, and again at this conference. The emphasis is on the scientific evidence and prevention agenda, and the overwhelming idea across the whole conference was that menthol helps the poison go down.

First of all, menthol is not benign. Menthol cigarettes are promoted as healthier cigarettes. Menthol cigarette smokers display poor mental health. Menthol inhibits detoxification of NNAL. Menthol inhibits cotinine clearance. It does stuff. It has unique sensory properties. The important thing here, again, with all these properties, it makes the poison go down. It is the ultimate candy flavoring.

They have greater addiction potential. And part of this isn't just what we're seeing as far as there is some toxicological thing going on in the body about menthol. It has to do also with the throat grab. The throat grab is very similar to that of nicotine. We have seen that in tobacco

industry documents. And that in itself is reinforcing. So if it's a menthol smoker who gets that throat grab, that's a reinforcing effect in itself. They are harder to quit; there is greater potential for relapse. And I think you take it from here.

DR. GARDINER: Thank you, Pamela. Let me just thank the Panel for having us.

I am Dr. Phillip Gardiner with the University of California; also, the president of tobacco-related disease research program.

I guess a lot of things have been thrown around yesterday, and what was most -- registered mostly with me was the question of the historic opportunity that this Panel has in front of us, and that we in the tobacco control movement face.

Let me just say that this is going to be an historic opportunity. It's going to be important for the Panel to step up and confront this opportunity directly. We do not -- I would encourage you, we do not need another 25 years of science before we do something about menthol.

Just to repeat, menthol cigarettes have been shown to be starter products for kids. Every speaker prior to me has actually said that. The most recent data from the -- SAMHSA itself has pointed out that naive smokers are the ones most likely to use menthol.

I think most telling is the FDA has already outlawed most flavorings already in cigarettes. There is no reason that they should not outlaw menthol. It is the same logic. There is no distinction in that.

Not only is it the ultimate candy flavoring -- Pam mentioned, a number of people mentioned -- it's a unique sensory reinforcement that goes on. The discussion on the street with menthol cigarettes is that you are not only addicted to the nicotine, you are addicted to the menthol. You are addicted to the taste of it. You are addicted to the taste buds that act. You are addicted to the cold receptors that come on. You can't disentangle them. They're all one thing.

Let me just say that the predatory and

relentless marketing toward the most vulnerable populations really makes this quite a social justice issue. If nothing else, if nothing else, it's important that this Committee -- actually, Dr. Henningfield asked, can you separate the marketing and the product? Let me suggest this to you that minimally this Committee could reign in the predatory marketing towards the most vulnerable, the most depressed, the most marginalized sectors of our society. It would be a great step forward for public health.

We have known that historically that African Americans, Asian Americans, Latinos, and American Indians, the poor, unemployed, women, and youth have been the target. Indeed, the bombardment of the African American community is historic. And while I appreciate the literature review that went on yesterday, it only began to scrape the surface of what has been done toward my community as it relates to menthol cigarettes. I think we have to do something. It is definitely a social justice issue of the first story.

A deleterious additive, as it has been stated by my colleague, Dr. Clark, this can't be reduced to solely a toxicological question; cigarettes already kill people. We know this. Even the tobacco industry admits that. What menthol does is that it makes the poison go down easier. I don't have any other great way to put it. We subtitled our report that we submitted to the FDA on that question.

In this regard, let me just say this. It is very important that we broaden the definition of harm. Now, we're going to say this a number of times. After the presentations yesterday, and also the discussion this morning, Dr. Clark and I are convinced that we will have to write something else on this topic in the next two months. There has been so many things that have said here, and they are so important.

But you have -- it's not just a molecular question. It is a question of initiation, addiction, harder to quit, greater potential for relapse. It has been the vehicle for the most

predatory marketing of the latter part of the 20th century, and led to the most deaths, frankly.

So our verdict, and we hope your verdict, is that at bottom, menthol makes the poison go down easier; and that we need to get all candy flavorings out of cigarettes. Menthol should be banned from all tobacco products, both those characterizing as menthol, and both the subliminal addition of menthol. And ban all menthol substitutes as well.

Let me just say this in closing. This is a tall order that we put before you. This is a major task, but it has fallen to you. If you are going to pick up the mantel and actually take up this historic thing, then you are going to have to take a chance. You are going to have to step forward and take the lead and showing us what's the best for public health.

To seize this moment, I encourage you to reduce the scourge of menthol and tobacco-related disease associated with it by eliminating this candy flavoring once and for all. Thank you very much.

DR. SAMET: Okay. Thank you, Dr. Gardiner

and Clark. I will say we heard about John Snow yesterday and today. For the record, John Snow, himself, did not remove the handle from the pump. He did make the recommendation once he had the science that suggested that was the right thing to do.

Clarifying questions. Greg.

DR. CONNOLLY: Dr. Clark, you presented a statement about the throat grab, which I -- I term that to be a chemosensory effect. Yesterday we had presentation on these thermal chemosensory effects of menthol on heat and on coolness. But when you use the term "throat grab" that appeared to me not a thermal effect, but rather more of a tactile affect.

MS. CLARK: Trigeminally, Yes.

DR. CONNOLLY: Let me ask the question. The first question is, that's not a thermal effect, that's a tactile effect?

MS. CLARK: Apparently, so. That's how the industry documents -- they talk about the balance between the nicotine throat grab, and the menthol throat grab. If you decrease the nicotine,

you increase the menthol, and it becomes reinforcing in itself; and that's very clearly stated in the industry documents.

DR. CONNOLLY: My second question, that throat grab is traditionally associated with the effect of nicotine or nicotine vapor on the post interferons. And what you are stating to the Committee is that menthol may serve as a substitute for that nicotine effect. That is, if you lower nicotine, you can compensate by adding menthol. Is that what you are saying?

MS. CLARK: Yes. That's the evidence in the documents. We're performing a study right now that is going to help us clarify that experimentally, rather than just relying on the industry documents that tell us that. Or essentially pain in the throat, anesthetizing the throat, and then not anesthetizing the throat in the menthol versus nonmenthol.

One of our problems is that -- it's a problem with all the epidemiologic literature -- is that cigarettes vary so much more than just menthol

and nonmenthol. And everytime we try to do a laboratory based study or an epidemiologic study that says, menthol cigarettes this way, nonmenthol this way; they are such different animals anyway. So what we really need is we really need a process for having absolutely identical cigarettes, menthol or not.

DR. CONNOLLY: Will that data be available within a year?

MS. CLARK: I will guess so, yes; probably.

DR. SAMET: Patricia.

DR. NEZ HENDERSON: The question is for Dr. Gardiner. Dr. Gardiner, in your presentation you used the word "social justice." In your own, I guess, interpretation, how do you think that tobacco industry was able to infiltrate African American communities where that now 83 percent of American -- African American population smoke. I mean, that's the part that is a little bit startling for me, that the numbers are so high among African Americans.

DR. GARDINER: Well, they made it a target

in the 1960's and '70's to penetrate the African American community with the menthol products. They say directly in their documents -- the article that I wrote in 2004, "The African Americanization of Menthol Cigarette Use in the United States," we used the industry documents that showed directly that they spent more money and TV advertising and magazine advertising aimed at the African American community as it relates to menthol cigarettes compared to any other cigarette. It became, for lack of a better term, quote, unquote, "our cigarette."

And increasingly we can say -- and I can do this, I believe, from memory -- in 1953, five percent of African American population smoked menthol cigarettes. By 1968, 14 percent smoked menthol cigarettes. By 1978, 43 percent or 42 percent smoked menthol cigarettes. And after that, it skyrocketed, and went up from 75, and now up into the 80 percent. So the targeted marketing of the most vulnerable and marginalized sector of the community bringing us candy coded flavoring to

bear. It is all in the industry documents. I'm not speaking out of school. That's in the history.

MS. CLARK: Can I comment on that, please.

DR. SAMET: I think actually, Pamela, we have very limited time. Jack.

DR. HENNINGFIELD: Two quick questions. First, Dr. Clark, most of the evidence of the most serious potential harms of menthol in cigarettes are with characterizing levels or in branded products. Yet, you recommended taking all menthol out. What is the logic or justification?

DR. CLARK: There is actually two issues going on. One is the predatory marketing and the branding of something and the advertising of it as being this cool and helpful thing in the characterizing ones. But in the other cigarettes, the non -- and most cigarettes have menthol in them -- it is really performing the same physiologic function. It is smoothing the smoke. It is making it go down easier. That's the reason it's there.

DR. HENNINGFIELD: And the second question is, in the town hall meetings and other meetings

that were -- everything that was associated with the national conference. I was at parts of the national conference, the town hall meeting. One of the areas of discussion that I don't have a good sense of, and maybe you can give us a sense, is can you remove menthol from the population of affected smokers without social disruption, backlash? You are making a recommendation. Can this be done, or how could it be done?

DR. GARDINER: Well, Jack, I think that's an excellent question. I think we should be aware up front of the consequences. If I read the literature correctly, and I think that it's harder for African Americans to quit smoking, that cessation is harder; and that they disproportionately use menthol cigarettes, then, it's going to behoove the federal government, and state governments, and local governments to put greater funds into cessation, straight up, in poor communities. We already know that these communities have the fewest cessation services available.

So I think any recommendation that comes

from this Committee has to come with some corresponding services that are applied to that. Clearly, there will be consequences. I am sure, as the industry taunts, there will be underground markets and people putting drops of menthol on their cigarettes. These things will take place. I guess I will say this, that the consequences that we have now are already horrific. I don't think that what we're talking about doing would -- couldn't even beginning to measure up to what's taking place now.

DR. SAMET: Last question. Dan.

DR. HECK: Just a quick clarifying -- clarifying question to Dr. Clark, or perhaps either speaker. We have seen a lot of mention of industry documents here and phrases within those. Should the Committee take those as representations on an equal basis with peer reviewed scientific published work, or are these -- this is information, but I wondered is -- do the speakers carry industry document quotations as an equal weight as peer review science?

MS. CLARK: I think it's really important

to replicate some of the really key points. It gives us an idea of what questions we should be asking, and what our suspicions should be.

DR. SAMET: I will just comment that I think this is a matter of how the Committee will weigh any evidence, regardless of source. I think this is a matter of our own process.

I appreciate your comments from both Drs. Clark and Gardiner. I think we need to move to our next presentation.

Michael Ogden from R.J. Reynolds Tobacco Company.

DR. OGDEN: On behalf of R.J. Reynolds, I thank you for the opportunity to present some brief remarks. I refer you to the extensive review of the scientific literature, which we submitted to the FDA on March 22.

As reviewed yesterday, there are no meaningful differences in the chemistry or biological activity of smoke from cigarettes with or without menthol. The bulk of the literature on smoking intensity measures simply does not support

the suggestion that menthol smokers alter their smoking topography in a way that increases smoke exposure. This finding is supported by the best available evidence on actual smoke exposure.

Regarding menthol and disease risk, the vast majority of data showed no differential effect of smoking menthol versus nonmenthol cigarettes. In the review presented to this Committee yesterday, there were at least three omissions from the literature that we believe should be pointed out and addressed by the Committee.

First, regarding the single study showing the statistically increase relatively risk of lung cancer in men, it was not pointed out that the authors of this study later considered their earlier result as a possible chance finding.

Second, was the omission of a metaanalysis published in 2007 by Worley (phonetic) that shows an overall nonsignificant relative risk of 1.01.

Third, was the omission of the 2008 study of Edsall that reported no significant excess risk of lung cancer among menthol compared to nonmenthol

cigarette smokers.

Thus, we agree with the published literature and summary of Heck that provides a substantial basis for a conclusion that the risks associated with cancers and other diseases associated with smoking menthol cigarettes are no different than those associated with nonmenthol cigarette smoking.

Regarding menthol cigarette use and smoking initiation, the published literature to date is comparatively limited. Two studies show no effect of menthol on initiation age. Regarding initiation rate, data from direct assessment through longitudinal studies do not exist; and that was acknowledged yesterday. However, using trend data for prevalence of daily smoking as a surrogate, one study demonstrated an overall decline in daily smoking among 12th grade African Americans from 1977 to 1998.

Importantly, the authors of that study note separately that survey categorization of adolescents and adult smokers differ. Adolescent

based surveys typically identify smokers as those having smoked all or part of a cigarette in the last 30 days. Based on a more accurate characterization -- I am sorry, categorization of current smoking, these same authors examined another data set and reported African American age specific rates of smoking initiation during adolescence were declining at all ages.

This Committee and FDA should not rely on smoking behavior data intended to be an early measure of smoke experimentation as an indication of current or regular smoking.

For emphasis, I point out the adolescent based survey categorization, which was relied upon entirely in one of yesterday's presentations regarding the NSDUH survey. There may be the impression that this is the only large and nationally based survey data set available with which to address this important topic; however, this is not the case.

We have identified three surveys, in addition to NSDUH, from which data are available for

reanalysis. Namely, NHANES, NHIS, and NYTS.

Importantly, the data are available and able to be a more accurate characterization of current smoking, and also enable comparisons across the four surveys. We are in the process of finalizing data analysis now, and we anticipate submitting the findings to this Committee for their consideration at the second meeting.

Without time to discuss the details, I note that the literature on menthol and smoking cessation provides conflicting results; and the two studies suggesting reduced cessation appear to indicate uncontrolled confounding by social and economic status. This makes it very difficult to determine conclusively whether there is any association between menthol smoking and differential rates of cessation.

The published scientific literature attempting to examine the relationship between menthol and smoking addiction or dependence is similarly inconclusive. A number of different addiction metrics have been employed inconsistently.

That, coupled with conflicting results from these published studies concludes any clear conclusions regarding an association between menthol smoking and differential age of addiction.

In conclusion, based on these comments and the more extensive review of the published literature submitted previously to the Committee, there is no scientific basis to treat menthol cigarettes differently than regular cigarettes. Thank you.

DR. SAMET: Thank you, Mr. Ogden, for your presentation. Questions from the Committee?

I might ask you, your submission and your statements were based on the published literature. Of course, our mandate extends to all relevant information. Would, for example, RJR have carried out work related to smoking topography and menthol, biomarkers, or other research that is relevant to the questions before this Committee that are not in the published literature?

DR. OGDEN: Yes, we have. Our understanding was that this meeting was to review

the published literature, which is the way that we limited it. We fully anticipate bringing those data forward in a fully transparent way at the proper time, which presumably could be the second meeting of this Committee.

DR. SAMET: Thank you. I mean, one of our tasks as we face questions will be to develop exactly what requests we will make to you.

Greg.

DR. CONNOLLY: I keep asking other people to go first.

Thank you very much for your presentation. Do you study your competitors' menthol brands regarding both their characteristics, their levels in the broader smoke or behavioral responses? So do you study your competitors' brands?

DR. OGDEN: As a general question, yes, we do. Maybe not in the specifics of the way you asked the question. Certainly, when we run comparative experiments of a cigarette brand or a new development, we often compare it to leading entrance in the market that might be a competitor. So it

certainly would be -- there certainly would be comparisons done on the chemistry, in vitro biology, and things of that nature when we look at a competitive brand.

DR. CONNOLLY: I have a second question.

You have recently introduced a new brand called Menthol Crush, which my understanding, has a pellet placed within the filter with menthol that allows the consumer to tacitly adjust the dosing of menthol. In doing that, did you examine the behavior of potential consumers in terms of their tactile use of the product, their chemosensory perception of menthol of that product?

DR. OGDEN: I'm not aware of any specific experiments. That's not my area of the company. I would imagine that we have. If there is data available, if this Committee would like to see them, I am sure we will submit them for your consideration.

DR. SAMET: Patricia.

DR. NEZ HENDERSON: Do you consider menthol a flavored ingredient?

DR. OGDEN: It is an ingredient by definition of the Act; and it does have flavoring; and the way I understand it as a consumer. So I think the answer to your question is "yes."

DR. NEZ HENDERSON: Yes. And one follow-up question. When the candy ingredients -- or the candy flavored tobacco products were on the market, were there any studies that you know of that increased the risk for diseases?

DR. OGDEN: I'm not sure I understand what you mean by "candy flavored" cigarette.

DR. NEZ HENDERSON: Just like chocolate flavored, pineapple flavored cigarettes. Did they increase the risk for disease?

DR. OGDEN: I'm not aware of any epidemiology study that would look at that type of cigarette to establish the basis for disease.

DR. SAMET: Neal.

DR. BENOWITZ: On the follow-up of the statements about no difference in risk between menthol and nonmenthol, and race issues in terms of lung cancer. Have you looked at the issue of

relationship between cigarette consumption and race and menthol? Because one thing that's been well documented, I think, is that African Americans have a particularly higher risk of lung cancer and low levels of cigarette consumption.

Of course, one question would be if menthol facilitates exposure, it would be most likely to be effective when you are trying to get a lot of smoke from your cigarette, which would be the case when you smoke fewer cigarettes. Do you have data to address the question of this interaction between cigarettes per day and menthol and cancer?

DR. OGDEN: We don't have any internal research on that point. I would acknowledge that, certainly, the high incidence of lung cancer in African Americans, in my view, is what started a lot of this debate from some years ago. The differential in that lung cancer rate has dropped quite significantly over the recent time course, while the proportion of menthol cigarettes has remained constant.

So I think there is a disconnect there

that requires further investigation by this Committee or other interested bodies.

DR. SAMET: Okay. Karen.

MS. DeLEEUW: Yesterday we heard a little bit of information about the idea that menthol smokers were much less willing to switch to nonmenthol than nonmenthol smokers to menthol. Do you have any data that would help us understand that?

DR. OGDEN: As I stand here today I am not aware of any internal data. Certainly, there is no research that I conducted. If we have data on that point and it would be helpful to the Committee, I would be happy to supply it.

DR. SAMET: Last quick question, John.

DR. LAUTERBACH: Dr. Ogden, I believe that Reynolds and other associated scientists have done some yield and use studies. I don't remember offhand whether they showed any difference between menthol or nonmenthol. Could you comment on that, please.

DR. OGDEN: I can. Yield and use study,

as I would define it, is an experiment where actually smoked cigarettes from smokers are collected and the tip of the filter is cut off and extracted. It has been shown to be a reasonably reliable estimate of the maximum amount of smoke yielded from a product.

We have conducted several studies, and they are not in the published literature, so I took them at a literal interpretation to be out of scope for this and would be delighted to present those data to the Committee at the next time. We have conducted three of these yield and use studies that have a menthol component. In all three of those studies the yield of smoke from menthol cigarettes tend to be reduced over nonmenthol cigarettes; and two studies are statistically significance; and one was not significant.

DR. SAMET: Thank you. And we will, I'm sure, be interested in seeing the data from those studies. Thank you, Dr. Ogden.

We are going to move on to our next presentation. Susanne Tanski, from the American

Academy of Pediatrics.

DR. TANSKI: Good morning. My name is Dr. Susanne Tanski. I am proud to represent the American Academy of Pediatrics, who funded me to make these comments today. The American Academy of Pediatrics, or the AAP, is a nonprofit professional organization of more than 60,000 pediatricians dedicated to the health, safety, and well-being of infants, children, adolescents, and young adults.

I am a pediatrician, and I am also an assistant professor at the Dartmouth Medical School and Cancer Center. In addition, I am an investigator with the Julius B. Richmond Center of Excellence. My research addresses message framing for tobacco cessation and smoke-free environments for children, as well as media influences on tobacco use among youth.

The AAP welcomes the opportunity to provide comments to the Tobacco Products Scientific Advisory Committee. This Committee has a vital role to play in the FDA's important work to protect children and the public from the harms of tobacco.

As you well know, tobacco is the leading cause of death and illness in the United States, causing more than 438,000 deaths each year. Some 80 percent, 90 percent of tobacco users started using tobacco products before 18 years of age. The connection between children and tobacco is so strong that Dr. David Kessler, then commissioner of the FDA, declared tobacco use a pediatric disease in 1995.

The AAP recognizes the substantial dangers of tobacco use and second hand tobacco smoke exposure to children's health. The Academy's Julius B. Richmond Center of Excellence, dedicated to the elimination of children's exposure to tobacco and secondhand smoke, was established in 2006 to foster tobacco control research and initiatives at the AAP.

The AAP believes that the FDA tobacco regulations should work towards the goal of eliminating pediatric tobacco use, addiction, and disease by controlling the factors that increase tobacco's appeal to children and increase their risk of dependence. The AAP applauds the FDA's recent

ban on cigarettes with flavors other than menthol, and encourages the FDA to move swiftly to extend this ban to include other products that appeal specifically to youth, including menthol cigarettes, cigarillos, Hookah water pipe tobacco, and smokeless tobacco products.

The Academy supports banning all candy and fruit flavored tobacco, and non-medicinal nicotine products. As the Committee begin its consideration of menthol cigarettes and dissolvable tobacco products, it will have to determine the criteria to evaluate the necessity of regulation. The Academy urges the Committee to adopt as its priority goal the protection of children from the dangers of tobacco, and the reduction of overall death and disease attributable to tobacco products.

In its review of menthol cigarettes, the Committee should not base its decision solely on the toxicity of the menthol additive itself. Rather, as discussed yesterday, the Committee should consider the impact menthol's flavoring has on the ease of inhalation, nicotine addiction, and the difficulty

of cessation.

The AAP believes that menthol and other anesthetics in tobacco are damaging to the public health and should be removed to prevent the next generation of children from becoming smokers.

In the event of a ban on menthol cigarettes, the Committee should also consider public health policies that would promote smoking cessation, and discouraging switching to nonmenthol cigarettes or mentholated smokeless tobacco products.

In its review of dissolvable tobacco products we also recommend that the Committee consider toxicity, particularly the potential for child poisoning, the risk of combining dissolvables with other tobacco products, their effect on smoking cessation, initiation, and use by children and adolescents, and their impact on nicotine addiction.

In addition, strong marketing regulation for these products is necessary to prevent casual initiation and addiction of youth who might be led to believe that these products have decreased risk

of addiction and harm.

The American Academy of Pediatrics looks forward to working with the FDA to eliminate child and adolescent tobacco use, and to reduce the public harm caused by tobacco. The Academy and our members hope to join with the FDA in public and professional educational outreach to ensure the protection of our children and youth. Thank you very much for the opportunity to provide comment.

DR. SAMET: Okay. Thank you Dr. Tanski.

Let's see, in terms of questions, I will say we have one more signed up speaker, and three who would like to speak for two minutes each. So if we are a going to accommodate everyone, I would suggest that the Committee be guarded in its clarifying questions.

So with that said, who has questions? Mark.

DR. CLANTON: Our previous -- at least two of our previous speakers advanced an argument that the definition of "harm" as it relates to smoking tobacco should be broadened. And then we certainly

have a statement as it relates to pediatric use of tobacco being a disease in itself.

Where do you put that -- sort of the beginning of that disease process? Is it in the initiation, or is it in the continual use, or do you parse that at all? Because this is going to be an important issue about where harm occurs, and, you know, how people interpret that.

DR. TANSKI: Absolutely. And I appreciate your comments. One of the biggest concerns about children starting tobacco use is that you can't tell by looking who is going to become hooked on tobacco. And we know from Judge Francis's work that it can take just a few puffs of a cigarette or just a few cigarettes before they show signs of dependence on nicotine. So if their first puffs of cigarettes are easier because of an anesthetic effect from the menthol, whether it's a mentholated cigarette or it is just the menthol constituent in a nonlabeled cigarette, and that makes it easier for them to have those first few puffs to get that nicotine addiction started, that is what we are most concerned about --

or one of the things we are concerned about.

DR. SAMET: Greg.

DR. CONNOLLY: You mentioned child poisoning. I would imagine it's infant poisoning, and the concern of the society. I'm just trying to understand that better. What type of poisoning, nicotine poisoning?

DR. TANSKI: Yes. Specifically, I was discussing the dissolvable tobacco products. And since the dissolvable tobacco products have come on the market, there has been an increase in poisoning. I believe that article has been published in pediatrics. It was done in concert with a poison control center in Pennsylvania. So the newest dissolvable tobacco products really do look like candy. They come in a little tin, and they are fairly difficult to discern from a mint.

DR. CONNOLLY: So what you are stating is that there is potential for risk for infants from poisoning from nicotine tobacco products?

DR. TANSKI: Indeed. It goes beyond infants to young children who are more capable of

accessing the little tins, for example.

DR. SAMET: Okay. Dorothy.

DR. HATSUKAMI: Yesterday in Dr. Rising's presentation he had showed that there were no studies that had been done on youth perception of menthol cigarettes. So my question to you is whether you know of any studies, or have you have conducted any studies on that particular topic?

DR. TANSKI: I have not myself done any specific studies on menthol, nor do I know of any specific studies. As was discussed yesterday, it's very difficult to do those. Because lots of kids when they have their first cigarette, they don't make a specific choice to try a Newport or a Camel or a Marlboro. It's the cigarette that their friend offers them.

Normally, they realize really what that first cigarette was when you ask them later. The best thing is to use perspective studies and find our specifically what they used for their first product. Those are ripe with confounding. The kids just don't recall what they used. So I don't know

of the studies. I do think it is going to be a challenge to choose that apart.

DR. SAMET: Okay. Thank you very much, Dr. Tanski.

Okay. We will move next to James Dillard from the Altria Group.

MR. DILLARD: Yes. Thank you, Dr. Samet. Good morning, everyone.

I am Jim Dillard, Senior Vice President, Regulatory Affairs for Altria Client Services. Altria Client Services provides regulatory support for Altria Group Incorporated's tobacco operating companies.

Certainly appreciate the opportunity to make brief introductory comments this morning on behalf of Phillip Morris U.S.A. I also appreciate the Agency's commitment to providing us with the opportunity to make a more complete presentation at the Committee's meeting this summer.

Phillip Morris U.S.A. actively supported passage of the Family Smoking Prevention and Tobacco Control Act for more than eight years, because we

believe a national framework thoughtfully implemented can contribute to resolving many of the public health issues that surround cigarettes and smokeless tobacco.

In implementing the Act, FDA has stated that it's decision making should be science and evidence based. We agree, and are committed to providing information at the FDA consistent with this approach.

Specific to this first meeting of the Advisory Committee, we provided a limited written submission and summarized the published scientific literature related to menthol. There is, of course, more to say on menthol; but our submission in my remarks are intended to address the Agency's request for comments on the published scientific literature.

To begin, we agree with the overwhelming medical and scientific consensus that cigarette smoking, either menthol or nonmenthol, causes lung cancer, heart disease, emphysema, and other serious diseases in smokers and is addictive. Let me also be clear, kids should not smoke or use any tobacco

products. We take this very seriously and have worked for many years to help prevent youth access to and use of tobacco products. Youth smoking rates have declined significantly since peak levels in mid-1990's, and are at their lowest reporting levels.

With regard to menthol, I would like to begin by highlighting published information from our own primary scientific work, including a study we call and -- conducted called the Total Exposure Study. This study was designed to estimate exposure to tobacco smoke, and to investigate the relationship between exposure and machine drive tar yield.

This study included nearly 3600 adult smokers, and more than 1,000 nonsmokers from 31 states across the country. Of those, approximately, 1100 were menthol smokers. We published on various aspects of -- excuse me, of this research, including a recently published paper, which investigated measures of exposure in menthol and nonmenthol smokers.

Also, we recently presented two menthol related posters at the recent meeting at the Society for Research and Nicotine on tobacco. The first analyzed the effect on menthol cigarettes on biomarkers of potential harm. The second analyzed the effect of menthol cigarettes on measure of nicotine dependence.

Our analysis of the published scientific literature, including our own work, indicates the following. Menthol cigarettes do not result in increased toxicity compared to nonmenthol cigarettes in nonclinical testing. Smoking menthol cigarettes produces no consistent effect on markers of exposure to smoke constituents, nor any consistent effect on human puffing or inhalation behavior.

There is no effect of menthol and smoking related health risks as reported in published epidemiological literature. Menthol does not play a role in smoking related health disparities observed between African Americans and White smokers. Menthol does not increase nicotine dependence based on currently used measurement methods.

Cessation outcomes are mixed, but do not support a conclusion that there is an effect due to menthol.

Finally, as it relates to smoking initiation, the research is limited and constrained by measurement issues.

Overall, the weight of scientific evidence indicates that menthol does not change the inherent health risks of cigarette smoking. For diseased risk as an example, evidence from epidemiologic studies suggest no effects of menthol. Moreover the difference in lung cancer risks between African American men and White men, if caused by menthol, should be seen between African Americans and White women, but it is not.

Our written submission provides more detailed information on each of these topics, including a list of references to published scientific literature, some of which were not included in the National Cancer Institute's Bibliography.

We also have additional published and

unpublished information, including on topics not discussed at this meeting, but which we believe are responsive and relevant to the Advisory Committee's consideration of menthol-related issues.

We thank the Committee for this opportunity, and look forward to future opportunities.

DR. SAMET: Okay. Thank you. Questions from the Committee. Patricia.

DR. NEZ HENDERSON: Thank you for your presentation, Mr. Dillard. My grandfather was a traditional healer, and over the years he began to mix commercial tobacco products with traditional tobacco, and that's what he smoked. He said that it masked the harshness of the cigarette. Do you believe that menthol does that to the cigarettes that you produce?

MR. DILLARD: I think that -- a couple of factors. Number one, we were here and were prepared to talk about the scientific literature today. I think there is information that as we move to the next Committee meeting, there has been a number of

questions that have come up, and we're certainly taking note of. I think that we are not in the best position today to comment on that; but in the future we would be happy to entertain those kind of questions from the Agency.

DR. NEZ HENDERSON: Will you provide information on the role of menthol at that time? Why it's used for your cigarettes?

DR. DILLARD: Yes. I think, as I said, the Agency will likely provide additional questions to the industry, where we will entertain those questions for any upcoming meeting.

DR. NEZ HENDERSON: Okay. Thank you.

DR. SAMET: Dorothy.

DR. HATSUKAMI: In this study that you had conducted looking at the differences in dependence between menthol and nonmenthol smokers, it appears that you used FTND, is that right?

MR. DILLARD: Yes, it is.

DR. HATSUKAMI: Did you take a look at the first cigarette -- the time to first cigarette in the morning? Did you take a look at that particular

item to see whether there might be some differences between menthol and nonmenthol smokers?

MR. DILLARD: Yes, I think, Dr. Hatsukami, you are referring to one of the paper -- one of the abstracts that we presented at the Society for Research and Nicotine. One of the conclusions that we have -- and I will just read from it. We are very willing to provide this to the Committee as well -- but adult menthol smokers have no increased odds of having higher Fagerstrom nicotine dependence scores as compared to nonmenthol smokers. And adult menthol smokers did not have increased odds of smoking within the first 30 minutes after waking, compared to nonmenthol smokers. So based on the work that is in the total exposure study, those were our conclusions.

DR. HATSUKAMI: I have a second question. In terms of the data on biomarkers that you had referred to from the total exposure study, is it possible to take a look at those biomarkers by certain brands, or at least the amount of menthol in the cigarettes?

MR. DILLARD: I think that's going to be very difficult, what I know about the total exposure study. That type of data will be very difficult to pull out from the study.

DR. SAMET: Greg.

DR. CONNOLLY: Two questions. One quick. Could you supply to the FDA the raw data for the total human exposure study relatively soon? I understand it is published. So as any published literature, to really look at that data, could you do that?

MR. DILLARD: I will go back to my earlier comment, Dr. Connolly, that, you know, if the Agency wishes to request any additional information that might be of value to this Panel or to the Agency, I think we are willing to entertain that.

DR. CONNOLLY: Thank you. My second question is, in the mid 1980's the Japanese cigarette market was opened. Phillip Morris became internationally -- became a very strong competitor in that market. At that time menthol sales were zero percent. Looking today, we are looking at

rates of approximately 20 percent menthol smoking in Japan. There was a very sharp increase in female smoking, 18 through 25 to probably 20 percent today. Do you think the introduction of menthol into that market increased the level of young female smoking?

MR. DILLARD: I can't answer that question. I think as you know as well, Dr. Connolly, the two companies have split. Altria is now the U.S. arm of Phillip Morris Products. Phillip Morris International is now a separate company. And I personally don't have the answer to that question as well.

DR. CONNOLLY: Just clarifying, at that time Phillips Morris --

DR. SAMET: I think this is pretty much off our point. Neal.

DR. BENOWITZ: I just wanted to ask what Dr. Connolly asked. And just to say there are a lot of analyses of interactions between menthol and race and cigarette consumption that, I think, require further analysis. And I would -- if at all possible for FDA to get that, and FDA to perform their own

analysis of this, just like when a pharmaceutical sponsor comes and wants to have a new drug approved they submit that data to FDA. FDA does an independent analysis. I think it will be very important that Altria provide the full data set so that FDA can do the analyses that we think should be done.

DR. SAMET: Okay. Mark.

DR. CLANTON: So when reporting no effect in the study, particularly looking at menthol versus lung cancer rates, or esophageal cancer, do you really mean no effect? Are you saying the studies are showing no additional effect on lung and esophageal cancer? The cancer still occur, and the rate should be similar. You are not saying no effect; you are saying no additional effect; right?

DR. DILLARD: That's right, Dr. Clanton.

DR. CLANTON: I have just wanted to clarify that.

MR. DILLARD: Yes.

DR. SAMET: Okay. Thank you very much, Mr. Dillard, for your presentation.

With the Committee's indulgence, we have three people who have asked to present. These would be presentations limited strictly to two minutes. I think we would not ask clarifying comments unless needed.

So I would ask the three individuals who have asked to make presentations to be near the mike, so we do not -- so we have Jim Tozzi; Jeanette Noltenhuis, Marcia DeFalco in that order. As you can tell, a very strict two minutes. That would be the warning. Mr. Tozzi from the Center for Regulatory Effectiveness.

MR. TOZZI: Good morning. I'm Jim Tozzi with the Center for Regulatory Effectiveness. Distinguished members of the Committee, I have just a brief message.

First, we see in the public that your Committee is an extension of the FDA. A very important extension, because you are addressing one of the biggest public policies that have been around Washington for a considerable time. To this end, we think it's important that you open up the

deliberation of your Committee to the public on a continuous basis. The important comments you got today should not be limited to comments every six months for two minutes.

So what are we asking? We are asking that you open this Committee up, because if you don't, I am afraid -- or we are afraid that any agency, including FDA, could dominate the proceedings.

So what do I mean by open it up? We think that this Committee, since it's going to be an established Committee, operate over a period of time, should issue some rules of governance, put them out in the Federal Register for public comments, and look very seriously for implementing something -- what we call in the repertory business an interactive public docket.

What that is, it's an automated web site where all public comments can be given to the Committee on a continuous basis, 24/7; they are public. Anyone that takes issue or disagrees with a particular topic can comment on it. Our web site -- if you go to CRE web site, virtually all our work

product is done through IPDs. Everyone agrees with us or disagrees with us can comment on it, and when our comments go to the federal government they are already peer reviewed by the entire public. People agree or disagree with us.

So I suggest that you open up this committee on a continuous basis to participation by the public. Thank you very much.

DR. SAMET: Okay. Next comment from Jeanette Noltenhuis, the National Latino Tobacco Control Network.

MS. NOLTENHUIS: Thank you very much for the opportunity, and thank you for taking on the responsibilities of this Committee. I am representing the National Latino Tobacco Control Network. That is 1400 community based organizations, researchers, and advocates working in Latino communities in the issue of protecting the public's health.

Just a quick note. I just -- I'm here to -- to echo what my colleagues in public health have said, that it is important to look at menthol

as a product, as an additive that changes the taste of the product, masks the harshness of the product, and facilitate the uptake for youth.

The marketing of this product has had an effect on all communities of color; and I -- this Committee has been charged on African Americans and Hispanic Latinos. I want to echo that it also has a very big impact on native Hawaiians, and Pacific Islanders, American Indians, and Alaskan natives, as well as Asian Americans.

And just to say that, yes, the scientific evidence is here and that's what you are discussing, I would propose that at the community level where people are seeing the marketing and living with it, and so on, that maybe this Committee needs to open up and have at least one or two public forums in which the community can participate. I think that you will actually get a different perspective. Not necessarily how you are going to make all of the decisions here that need to be made -- and they certainly have to be made with scientific research done; but a lot of research hasn't been done in

terms of how --

DR. SAMET: Okay. Thank you for your comments.

MS. NOLTENHUIS: Thank you.

DR. SAMET: Next, Marcia DeFalco from General Dynamics IT.

MS. DeFALCO: Good morning. My name is Marcia DeFalco, and in the interest of full disclosure, I do work for the Health Information Technology Division of a $29 billion General Dynamics, and they may have some contracts doing infrastructure for tobacco-related companies that I'm not aware of.

I have several advanced degrees, but my discipline -- in my discipline, but they are not health related. So I will restrict my comments to my field.

I have worked for more than 25 years in and for two regional health care systems with cancer, mental health, and substance abuse programs. The Military Health System, the Veterans Health Administration, and Health and Human Resource --

Health and Human Services Operating Divisions in various corporate and nonprofit communications and marketing positions.

I am personally ecstatic that CTP has been created, and have tremendous respect for the work that you are doing on behalf of the public. In my professional marketing experience and based on my industry studies, getting your research and data out to the public in a timely manner is critical. CTP should continue to do what you are doing in terms of sharing and correcting data in information, conducting media and web searches to find and correct outdated data, and to continue to identify best practices in commercial and government sources, including sister organizations, such as what CDC does with cutting edge social media outreach to communities of color, web site and call center coordination, and other examples that you can find with Whitehouse.gov, and 1-800 Medicare.

For example, a timely opportunity exist this weekend that your media professionals may already be aware of. "60 Minutes" is doing a

segment on menthol products.

DR. SAMET: Okay. Thank you. I'm sorry, you are out of time. Two minutes goes by quickly, doesn't it?

Let's see, this -- the open public hearing portion of this meeting is now concluded, and we will no longer take comments from the audience. The Committee will turn its attention to address the task at hand, giving careful consideration of the data before the Committee, as well the public comments. I do want to thank all the public commenters for your efforts and the materials you have brought before us. I am sure they will be helpful to us.

We are going to take a break. Let's see, we are a little bit behind. If go for 15 minutes, that's five of. I need to remind the Committee, no discussion of the meeting topic during the break amongst yourself, or with any members of the audience. So back at five of. Thank you.

(Whereupon, a recess was taken.)

DR. SAMET: All right. We're going to go

ahead and reconvene. Because we do want to break -- we need to break right at noon for lunch. I think a number of Committee members still need to check-out. So we will -- we will do that.

Now, we're going to begin the Committee -- begin our discussion and answer the -- address the questions -- not answer them -- address the questions put to us, the four questions that have -- are the focus for our discussion this morning and this afternoon. I think, Corinne, you are going to get us started on this discussion.

DR. HUSTEN: Thank you. As you know, there are the overarching questions that eventually you are going to -- not eventually, but in 12 months that you are going to have to answer about the menthol and public health, take into account it's use by different populations, and any recommendations you would like to make to us.

As you remember, there were those other provisions that you specifically need to keep in mind as you are thinking about it, including its impact on both users and nonusers; the impact on

beginning to smoke, stopping to smoke; the feasibility of any recommendations; and you know, any potential consequences, you know, such as contraband, or things like that.

So, you know, it's not -- we didn't put those questions before you today, because those are the questions, ultimately, for the report; and you don't have, as we have heard from all of you, the information that you think you need in order to answer those questions. So we had more focused questions for this meeting that we would like you to address.

Again, just to remind you, one -- and I think we heard a little bit of discussion about it -- but what are the specific questions around menthol that you would like the industry to address in the next meeting? Because we do want to leave time at the next meeting -- a fair amount of time for industry presentations.

Secondly, what other information do you think you are going to need in order to meet the statutory requirements of this report? And we heard

some thoughts about that during the clarifying questions. But I encourage you to think about, especially, what you think is the critical information you need. You know, give us some sort of prioritization. Because I heard lots of things that you might like, but it would help us to know which of the ones that you think are the most critical questions that we should be focusing on, or the most critical information.

What agenda items would you like to see included in future meetings? And then the last question is just, what other support do you think you are going to need in order to get a report done in 12 months?

So we do want you to consider all four of these questions at this meeting, and hopefully give us guidance on all four of them so that we can craft the agenda for the second meeting, think about the agendas for the future meetings and have in place, you know, our processes -- or put into place processes to help you complete the report.

Any questions?

DR. SAMET: Just to -- Corinne, just to clarify, you might remind us in terms of the questions that might be addressed to industry, and what industry needs to provide? What is the mandate under the law in terms of either, for example, providing raw data, materials that have not appeared in peer review literature to date, or other information that the Committee might not want to consider?

DR. HUSTEN: I think there are two avenues open to you. One is, you can make the request for what you would like industry to present at the next meeting. That's voluntary, and you know, the industry, as I said, can take it under advisement and come in with their presentations.

The other option is that we do have an ability to request information from industry. I would ask you to think, you know, carefully about the types of information that you want, because of the limited time frame that we have to synthesize any information that we get, you know. I would ask you to think about, you know, what is the critical

information as opposed to all -- potentially all documents potentially available to you. And part of that is the feasibility question, because of the report needing to be done in a relatively short period of time.

DR. SAMET: Greg.

DR. CONNOLLY: Just two clarifying questions before I respond to the question itself. The first clarifying question is, we have digested an awful lot of material, and I am so confused right now. Before coming I thought I was confused before. And really to make a rationale scientific decision, I think careful thought has to be given. If we want to present information today; but are we able to present to Cristi written materials -- written questions within a reasonable period of time, sort of summarizing responses to your questions?

DR. HUSTEN: Actually, I will ask Karen the procedural question. I mean, the debate, you know, needs to happen in public, in terms of, you know, are you making your decisions and coming to your recommendations? Purely administrative types

of questions, I think, can go through Dr. Samet to us -- Karen.

MS. KAREN: Cristi.

DR. HUSTEN: Through, Cristi, Sorry. Through Cristi to us.

You just have to be sure that anything that is a more content specific thing occur in the public meeting; and if it's purely administrative, you can let us know.

DR. CONNOLLY: Then, the second point of clarification is, you know, for us to compare apples and apples when we have presenters, I think it's important that we look at procedures. I don't want to use the "term" standards that are allowable within the context of the law that, perhaps, a drug manufacturer may be looking at. That is, do we first look at characterization. Then, do we look at clinical effects? Then, do we look at behavioral effects? Do we look at epidemiological? Do we have post markets and so on?

I don't think it's necessarily our job, but if you can think of structure, it would be an

awful lot easier than to insert questions in. So that's just one comment for the record.

DR. HUSTEN: I will just say it would be helpful -- we will, you know, ultimately, obviously, decide what we're asking for. It would be helpful to hear from you at this meeting what information you think would be helpful to you; and then, you know, we can then look at it and think about it. But I think part of the reason for putting this question out here was to hear from you what information you think is important.

DR. CONNOLLY: Well, the clarifying question was I think we need standards and procedures before you begin to insert questions. And maybe we should be also talking not only about the questions we want to ask, but, also, what is the procedure, what is the structure for asking those questions? So that we are comparing apples and apples when presentations are being made to us.

DR. HUSTEN: I guess I would say if you have thoughts on that.

DR. SAMET: Actually, John, I thought you

were going somewhere else with your comments. I think one of the things I think we need to think about in formulating our answers to the -- these questions, which in part relate to planning our next meeting and making sure we have the information we need is, what might the form of our report, in fact, be? And as we move towards conclusions, bottom lines in that report, how might we express them? I think we might want to give some thought to that as we -- as we talk today.

I mean, some of us around the table have worked on various forms of systematic reviews, whether Surgeon General's report, NCI monograph, or other kinds of documents. I think we need to think about what the shape will be for our report. What evidence we want. How we are going to bound the evidence that we want. I think that relates to these questions.

Clearly, we could identify a far larger body of data than might be digested by FDA and this group over the year that we have. So I think that we're going to have to draw our target for

identifying evidence carefully. That, I think, ought to be said in light of where we want to be, and how we will be able to have an evidence based conclusion in the report that sets out the evidence in a clear, transparent basis for reaching the -- a conclusion. Jack.

DR. HENNINGFIELD: Two things. One to Dr. Husten and one just to follow-up to Dr. Samet. Most of us have worked on a wide range -- I think at one extreme is the Surgeon General's report process that takes years. The other extreme, perhaps, is World Health Organization, couple page recommendation. I expect that we are someplace in between, but that is something that we need to give thought about.

My question to Dr. Husten is related to industry documentation request. And I'm wondering to what degree will similar procedures be followed as this will be carried out in the Center for Drug Evaluation and Research at FDA? In other words, if there is a sponsor -- where there were questions from a meeting about a specific effect with a

specific substance, what, generally -- the Agency will specify what form they want it in? What specific information -- it is not open ended. So probably not helpful for anyone to have a huge data dump. What kind of --

DR. HUSTEN: I mean, we will need to make any request provided for under the statute. So what would be helpful is you tell us what you think will be important, or what you think will help you make the decision. Then, you know, we will work within the constraints of the statute to get you information that you would like to have.

DR. HENNINGFIELD: Are there -- so that would include the timeliness. We have to have a report in here. So getting a data dump in 11 months wouldn't be helpful. So that's something that the Agency will need to think about, and I think we all need to think about being as specific as we can what exactly we think would be nice or is critical.

DR. SAMET: Just to follow-up on Jack's question, Corinne. If there was a need for some form of data analysis, whether that was -- I guess

additional survey analysis or data analysis might be done by CDC. If, for example, data sets -- the Total Exposure Survey or some other study, broad data were delivered right now, does the Center have the capacity to do analysis, or to make arrangements through consultants for it to be done?

DR. HUSTEN: We have some mechanisms that we can use. Again, you know, we're a new Center. So, you know, we -- there are things we can do. There might be issues with, you know, huge volumes of material. I mean, we will do our best to -- again, within the statute, and what we are allowed to get and not get, and within the constraints that we have. Again, if you can prioritize, that just helps us.

DR. SAMET: Okay. Mark.

DR. CLANTON: As you can see, we're struggling on how to even answer some of these questions. So I don't know, for example, how marketing data is looked at in other scientific panels, or whether it is looked at, at all. In this case, and I think under the statute, marketing data

is kosher. We can get it; we can ask for it; we can use it in our deliberation. So do you have any comments on how marketing data is or isn't used in other panels? Maybe some guidance on how we might ask questions about marketing data.

DR. HUSTEN: I actually don't know how marketing data is used by other panels. We're happy to find that out and get that to you.

DR. CLANTON: Yes, that would be very helpful. Because we can look at marketing on one aspect, which is look at epidemiology and look at who buys something or finds something attractive. If there were documents in the design of a marketing approach that say, we're going to create a package this way and add color in this manner and represent it to the community in a particular way. If there are documents that are available, we want to see those. Then, that will tell us a lot about which audience or what some subpopulations things are being marketed to.

DR. SAMET: I think just one other matter of clarification, and I don't know if this is on a

slide, but this is from the Act itself around the scope of our charge in the menthol report. And I will just read. So I'm reading now from menthol cigarettes -- I'm not good enough to know what section. 907; thank you, Cristi. I'm sure this will all become second nature.

Just reading it says, "immediately upon establishment of the TPSAC, the Secretary shall refer the Committee for report and recommendation under Section 917(C)(4) the issue of the impact of the use of menthol in cigarettes on the public health, including such use among" -- it goes on to name different groups. So we had a little bit of this discussion yesterday. The difference between -- here it says use of menthol in cigarettes as opposed to menthol cigarettes. And do you have comments on this, I think, very critical distinction? I'm just literally reading the language here where it says "use of menthol in cigarettes."

DR. HUSTEN: And you have the same language we have. I would say that you should base

your recommendations on the science.

DR. SAMET: I will say in terms of our discussions, much of it, in terms of the public comments today and presentations yesterday, had, I think, largely a focus on menthol or mentholated cigarettes, as opposed to use of menthol in cigarettes. Clearly, use of menthol in cigarettes encompasses mentholated cigarettes, but it potentially extends more broadly.

Let's see, Melanie.

DR. WAKEFIELD: I had a question where I was going to plunge into the first question, but I think we're still kind of --

DR. SAMET: We will the come back. So any one to this point? John.

I think, actually, just a reminder, both cell phones should be off. If you turn your microphone off after every utilization, I think we will avoid high frequently hearing loss.

DR. LAUTERBACH: Dr. Samet, I think one of the things that we seem to be lacking -- we, certainly, referred to some of the testimony -- is

really contemporary data on levels of menthol use both subliminal and as mentholated. There is very little data in the literature of anything contemporary, and that would certainly be helpful. We have heard that 90 percent of products contain menthol. That's a little bit different from my memory; but then I haven't seen any really good data in five and a half, six years.

DR. SAMET: Actually, on my list of items that we should request from industry is information on the distribution of menthol use across all cigarettes to understand that. Greg.

DR. CONNOLLY: Just to expand on what you just stated, John, is the Act does say the use of menthol, but it's preceded by the term "the impact." And I think that term "impact" on the public health, or -- as essential as use. And the definition -- and the Act then goes on to define impact on public health in very specific terms. I think that provides us good direction in terms of how we approach the report.

I can say that yesterday I was impressed

with the FDA's structuring of their presentations relative to the impact on public health. I think those are -- in my opinion, those provided, you know, a fairly good area to base the report on; and I think you probably should ask of members, are there other areas that should be addressed? Are there areas there that you may not think applicable. And it's probably not part of this discussion right now. It may come up, you know, later; but, again, it comes back to the concept of, you know, what is the structure of the questions as it relates to presentations of scientific evidence; and then, finally, the construction of a report.

DR. SAMET: And certainly, I think the word, "impact," again, as I mentioned yesterday implies that the use of menthol in cigarettes leads to something possibly different from what would have been had there not been menthol in cigarettes; and that's, you know, again something that we will have to think about how one would determine what the impact is beyond aspects of toxicology, you know, sensory stimulation, et cetera. Dan.

DR. HECK: Yes, I guess I hadn't really considered that in this level of detail. I will certainly consult with the represented companies to see if there are opinions or diversity of opinions. I guess my going in impression was that we -- the intent here was to address the exclusion of menthol from the otherwise ban of characterizing ingredients, which I think the definition of flavor is borrowed directly from the food definition of characterizing flavors.

I do think we will need to get some clarification from FDA of their read on, are we talking about any use of menthol, or the characterizing use as what we traditionally think of as a menthol cigarette, very, very distinctive flavor and aroma? Again, almost directly borrowed from the food statute.

DR. SAMET: I suspect that I'm not -- probably, the clarification may well come from this Committee in our discussions of the language that's in the Act, I think. Dr. Clark, did you --

DR. CLARK: Yes, as a lawyer I would

suggest what we should do is check with FDA counsel, and a legislative person who should check with the Congress their intent. Because as was pointed out, we need to get the legislative intent. It seem to me -- I agree with Dr. Connolly -- this is fairly broad; which would include information from menthol period, to mentholated cigarettes. But that may not be the intent of Congress. I think you do need the specific prerequisites in order to establish what kind of line of reasoning you are going to pursue.

So I think that is a very important first step, given the confusion that we have about the distinction between menthol cigarettes and menthol in cigarettes.

DR. SAMET: I'm not -- just to be clear, though, I'm not sure that we're confused necessarily. I mean, I think the language is quite explicit. I think the issue is one of interpretation of the language. And I think in terms of this question of impact on public health, we may need to make a determination based on the evidence available as to whether there is impact

both of menthol as an additive, in general; and mentholated cigarettes. They may be two separate determinations from the public health scientific perspective.

DR. CLARK: That's the point I'm trying to make. If all the research was on mentholated cigarettes as opposed to menthol in cigarettes, if a large percentage of cigarettes have menthol in it, but they are not -- it is not substantial, then the stuff we were given yesterday was not targeted to that. So that means you need another body of evidence to pursue the question of the impact on the public health.

So in order for staff to -- FDA staff to give you what it is that you need as background, you need that distinction to be resolved.

DR. SAMET: Correct.

Jack. You were next.

DR. HENNINGFIELD: I think we have enough understanding to, at least, move forward. We have to make sure that the final report addresses the issues; but, also, I think we have -- we learned a

lot yesterday that will help us move forward with what areas are probable areas of harm. So probable area of harm that is probably pretty obvious is increasing smoking in African American youth. That's an area that needs to be considered.

Whether or not you have a large section of the report on the toxicological or the increase of menthol, whether it increases cancer risk directly that did not look like a fruitful area, major area? I'm not saying it shouldn't be covered. I think even at this point we have learned a lot that tells us about potential avenues of public health harm that would allow us to focus our efforts.

DR. SAMET: Ursula.

DR. BAUER: We didn't hear a lot about dose yesterday, and this statement that menthol is in 90 percent of cigarettes, I think, has been swirling around the discussion. If some menthol -- and we don't know how much -- is important to health impact, then, that may be one of the reasons why the literature is so unclear in terms of various impacts of menthol. Because, in fact, every smoker is more

or less exposed at one degree or another to menthol.

So I think that's a key piece of knowledge that the industry can help us understand is what is the distribution of menthol across cigarettes?

DR. SAMET: I agree. I think, perhaps -- actually, Cristi, as we develop these lists, do we need to come to sort of a voted agreement on what will go on, how do we -- whatever we want?

Maybe we could just begin to make a -- at least a tally of things that we think are things that we need. I think, certainly, I echo your statement that it would be useful to understand the distribution of menthol use across products. That really refers to the amount in the products, whether they're a, quote, menthol cigarette or not.

Let's see, I think, Dan.

DR. HECK: We may have gone beyond my comment, but I guess my plain language reading of -- at least in terms of ban of characterizing flavors in the original statute, would seem to suggest to me that we -- probably the initial focus -- maybe exclusive focus should be on that characterizing

use, you know, a real menthol cigarette; but again, I guess, it's a lawyerly interpretation.

DR. SAMET: I think, Jack, go back to you.

DR. HENNINGFIELD: And Corinne -- Dr. Husten, this is also a question related to charge to the Committee. We are assessing public health harms, and so forth. Are we also suppose to be making recommendations for what might be done? And if we're making recommendations for what might be done, then, in principal, you could say the evidence for harm is on this basis of science at characterizing levels.

That would not preclude a recommendation -- if that's the case, recommendations could range from restricting characterizing levels to restricting all levels, or any number of possibilities. You don't have to have evidence on a low level to restrict a low level. That gets into feasibility issues. For example, how feasible would it be to restrict just higher levels?

To what degree are we making -- should we be making -- thinking about specific recommendations

for what might be done?

DR. HUSTEN: Well, the questions that I put to you for the report are the -- pretty much taken from the statute. And so we need you to use that language as far as deciding what you want to put in the report. Again, you're a scientific advisory committee. So based upon your understanding of the science. So we are not going to put any priority restrictions -- you know, the questions are the statutory questions, and that's what we need you to look at. And there were those caveat of things you were suppose to take into account.

DR. SAMET: John.

DR. LAUTERBACH: We have heard various witnesses talk about this candy effect. While it's been several years since I smoked a menthol cigarette, I don't remember it being candy. Are there other descriptors coming in that we need to consider and ask industry for some information on?

DR. SAMET: Greg.

DR. CONNOLLY: Could that be part of our

recommendations of questions to be asked from industry? You know, I think -- I would like to delineate a time period when we can present that, and I think I'm prepared to respond to your question; but I'm not sure if it's the appropriate time.

DR. SAMET: I'm not sure I understood the question. I don't know if others did. I mean, we are speaking specifically menthol. You raised the issue of candy. Can you clarify perhaps, Greg. You understood the question.

DR. LAUTERBACH: Several witnesses here have characterized mentholated cigarettes as candy tasting, which I would assume more like a peppermint or spearmint, not menthol. So, obviously, there is some sensory information out there, apparently from some source, saying there is something else going on.

DR. SAMET: Okay. I think we're, obviously, going to be interested in studies of sensory perception. That may well be on our list of items to request.

Who else do we have? Melanie.

DR. WAKEFIELD: I'm not sure if this is relevant at this point, but just following up on your comment. I mean, there are lots of brand descriptors that -- that sort of describe menthol, I suppose, and that are used by the industry in marketing and words like fresh, mint, icy, cool, and so forth are all kind of words and adjectives that is -- are used in marketing. And those kinds of words elicit expectations in consumers. And so I'm quite interested in looking at documents in relation to consumer studies in relation to consumer perceptions of menthol, but also of some of those descriptors that are associated with menthol as well. Because I think, you know -- and consumer's kind of health related beliefs or expectations about what the cigarettes might taste like.

DR. SAMET: Can I make a suggestion that what we do is -- I think we are sort of going there -- is focus in on responding to the first question, which I think you are after. I suspect that we need to be as specific as possible in our

request for what industry should address at the next meeting. I would anticipate that, perhaps, there are substantial bodies of data that they may have that's relevant. And I am sure to the extent that we can focus in and be very specific we should do so.

Let's see, can we keep a running list. Okay. If you could do that, Cristi, I think that would be helpful. I think we could try and shape this with enough precision that we can hopefully turn over a useful list to the industry. Dr. Clark.

DR. CLARK: We can start off with a basic question, why does the industry put menthol in cigarettes? I mean, they are in the business of making money. They must have a motive. Is this somehow related to their desire to make money from this product? So I mean, it's a fundamental question. If you are going to ask the industry questions, I would start with that question. Because they have got to have a logic or a rationale.

DR. SAMET: I think that's consistent with

our mission of identifying the scientific evidence that -- to understand how menthol acts to fulfill our mission. I think that's -- should be -- it should be implicit. So if I have -- one thing that we want on our list right now, we have our distribution of menthol across products. I think it would be framed quite specifically.

Then, Melanie, let me go back to you to maybe frame things while we have -- so we can get something down. Then we can get to you. I think we are there now.

So we are shaping now our response to question one. Try to do this with enough specificity that, in fact, we will see the types of evidence that we think will be most useful for our report. So that's the overall goal. So we have one for starters. We have one thing. Okay.

Okay. So we have the distribution. Then, let's go back to Melanie's, and work on that. What I suggest is we do sort of one at a time, everybody who has things, keep them at the ready and we will get to them.

So, Melanie, do you want to go ahead.

DR. WAKEFIELD: Sure. It might be helpful if I just give you a little context for this; and I will be just quite brief.

In many countries where lights and milds have been banned, the industry has used other terms, other descriptors that kind of have similar implications in terms of adjectives for light and mild. If we were to go ahead and limit or ban menthol, the industry could well go ahead and use other terms that connoted menthol; and those terms and things like mint, and fresh, and icy, and so forth.

So I'm very interested in understanding what kind of consumer testing studies have been done on smokers and young people's expectations about the taste of menthol cigarettes, and also the potential harm or benefits, protection in relation to harm that menthol might confer, or menthol like descriptors.

DR. SAMET: Okay. So let me -- I think I heard two things. One might be studies of

perception; and second was studies -- studies, actually, of perception when exposed to smoke. Then second to that was consumer perceptions of what a product provides in terms of taste. There are potentially two types of studies that might have been done.

DR. WAKEFIELD: There's three. Third would be perceptions in relation to advertising claims and packaging claims.

DR. SAMET: Okay. So we can list all those. We may need to come back and give priority. Particularly in light of our ultimate mandate.

Okay. Good. I think, Dorothy.

DR. WAKEFIELD: Just Cristi, and also in relation to packaging claims, not just advertising claims.

DR. HATSUKAMI: Just to elaborate on Dr. Wakefield's comment, it would be nice to see it among users, as well as nonusers. Consumer perception among users and nonusers.

Also, to elaborate on what Dr. Bauer had said, it would be interesting to see the

distribution of menthol across the whole range of cigarette products, and changes that have occurred over time as well. So having an historical perspective as well as what is currently -- what, the current contents are.

Also, I would be interested in looking at -- more in depth on the studies that were presented by Altria, the biomarkers of total exposure studies relevant to what Dr. Benowitz had said, looking at it by gender, by race, and by menthol versus nonmenthol cigarettes.

DR. SAMET: Actually, Dorothy, just in terms of instructing Cristi here, do we really want biomarker studies? We heard about one particular study that might be particularly informative. We would be interested in the results of unpublished, because we know that some are published. NHANES has a paper out, for example. So we would be interested in the results of unpublished studies of biomarkers in relationship to menthol, if I understand it; and particularly the study presented by Altria.

DR. HATSUKAMI: Right, and by subgroup.

DR. SAMET: That might require analysis of raw data, or perhaps, that could be done. We could make that request.

Let's see. Since Cristi is tied up, I have lost absolute track of who wants to comment. Let's see, let me -- I think start left, if that's all right, then go right. Neal.

DR. BENOWITZ: I think it would be nice for us to get a picture of the manufacturing process. I would like to know where the menthol comes from, the various sources. How you manufacture a mentholated cigarette. What the quality control is. How consistent it is from pack to pack, from year to year.

I would also like to see data relating to menthol deliveries versus ventilation, correlations of menthol across cigarettes with nicotine and tar delivery. I just want to get a sense of what the mentholated cigarette product is about.

DR. SAMET: We may need to get that a little more specific, but I think as a start we can come back and discuss that. Let's keep making this

round, and we will see what we have got. Karen.

MS. DeLEEUW: Yes. I would be interested in getting a little bit more information about what the industry knows about switching from menthol to nonmenthol cigarettes.

DR. SAMET: Mark, are you --

DR. CLANTON: Actually, both Dr. Wakefield and Clark made specific my earlier request for marketing data. There are database reasons why there is menthol in cigarettes. Why they are at particular levels. We would really want to see those reports, so we can understand the intention of putting it in there, putting in their potential levels, and then shaping products around those data. You guys actually did a better job of asking my question -- or my request than I did.

DR. SAMET: Jack.

DR. HENNINGFIELD: I expect there will be some overlap, and the FDA will sort out these questions. But I think it would be very helpful to have quantitative data from each manufacturer on what has been added to their brands over the years;

and the measures that I would be interested in are total amount per cigarette and concentration. There are other things too, but I think that's a starting point.

The second -- and this overlaps to Dr. Benowitz's point -- but this qualitative description. I am still trying to figure out what is the family of substances referred to as menthol as based on what the cigarette companies actually put in? It may not or may not be the same across brands. This relates to the definition of a menthol cigarette. How does the industry define menthol?

What are potential analogues or substitutes for menthol that should be considered in an approach to dealing with menthol from the industry?

What are the dose-response curves for behavioral and physiological measures that the industry uses to set the dose of menthol? And the FDA in it's '95, '96 investigation found an amazing consistency in product constituents, I believe; including menthol. What determines that? What are

the variables?

Dr. Heck mentioned yesterday that you have to increase menthol to get the effect in a light cigarette. What are those effects? So what are the dose-response curves?

How do dose-response curves vary by gender, ethnicity, and age? Again, we saw data on differences in different brands, something must be helping the industry make decisions as to how much menthol they put in. It's not random, I assume.

What is the threshold that the industry has determined for producing a characterizing effect? What data -- dose-response data does the industry have for what I'm going to call right now low levels of menthol? Because, again, something must determine how much -- why put it in if it doesn't do something? There has got to be some data on the dose response on what those subcategorizing levels are doing.

Benefit. Is there any public health benefit that the industry can identify? I think that's important, because toxins are approved all

the time, but generally under certain conditions and when there is a benefit. I haven't heard a public health benefit. If there are no benefits, then, it's difficult to justify risk.

And the last is -- gets to more marketing. How -- on what data does the industry used to take a menthol brand off the market? So if it puts a menthol brand on the market or uses a particular type of menthol, on what basis does the industry take it off? And this would get into consumer perception, I think, that's already been talked about.

And finally, a question was raised about switching from menthol nonmenthol; but what information does the industry have on attracting nonmenthol smokers to menthol? In other words, what kind of people are sought after? What kind of people do you get? This is pretty basic, I think, in any marketing.

DR. SAMET: Jack, just one question. Your very first one is the same question about obtaining information on menthol in cigarettes. What time

domain do we want? Let's think about that. Just get some clarity. Probably don't need to go back to start. Just to keep us from being overwhelmed, and FDA from being overwhelmed. Do we want, say, the last ten years, or some snapshots so that we can understand recent trends?

DR. HENNINGFIELD: It may be that we want it in batches. I think we certainly want the last two decades or so. This has been a period of tremendous growth. Introduction of brands, and brands have come off the market. But, in principal, I don't know why we should not have a simple chart. Every company must have it; but what brands are out there and how much since they started?

DR. SAMET: We will come back. I think some of this might help. Continuing on down. Patricia.

DR. NEZ HENDERSON: Jack, that was very thorough. I really don't have anything to add other than to get more information on how the industry has -- marketing strategy towards African American communities, as well as the Latino communities, and

money spent on advertisement. Everything that we could know to have a better idea of what is happening in terms of marketing among these communities.

Also, this is going to have a huge impact on American Indian Tobacco Industry. So I would like to know which industries in American Indian are producing menthol cigarettes.

DR. SAMET: Okay. Greg.

DR. CONNOLLY: I just would probably try to expand upon previous comments. On Monday we were told that, you know, we are similar to other scientific advisory committees with FDA, you know. Therefore, went back and thought, well, how does that behave relative to a drug company? Just trying to structure things. I would be interested in -- I think many people talked about the characterization of menthol. I would be interested in the effects of menthol. I would be less interested in the safety issue. We look at drugs. We look at safety. Because we know cigarettes are harmful.

Then I would be interested in looking at

those effects with clinical research; and I break down to three areas; chemosensory would be a clinical research. What is the effect on chemosensory perception? Neurobiology. What is the effect on the neurobiology from head and neck receptors that are affected by menthol? Behavioral.

I would then go to marketing research. I would be very interested in marketing research of brands. And then finally post-market surveillance. So those are the categories. Characterization. Clinical effects, marketing, then post-marketing effects.

I think in looking at the question one must ask the question of data sources. One, in terms of characterization, I think the data sources could go back 20 years; but in terms of the entirety of the data, I would not set time limits.

Data sources, I think, have been well established through industry through the MSA; and I think those are appropriate. There are certain limitations that I would reference. One, proprietary information; and I think that should be

protected in accordance with the law. But I don't see why internal staff who have taken appropriate precautions should not receive proprietary information.

Research done in foreign countries oftentimes wasn't reported to FDA. I think research done in foreign countries that is not in the MSA resources are something one should consider.

Characterization of a product -- and I'm just expanding on what Dr. Clark would say, what Neal had said. I think we have to know, one, is menthol essential to smoking? Why is menthol used? Then we get even deeper; what are the types of menthol we are talking about?

I would add, Neal, how is it delivered? Is it delivered in the paper, in the rapper, in the filter? Then we want to know is it natural or synthetic? I think we also want to know -- this is at a subbrand level -- menthol content in the rod, and then menthol content in the smoke.

One could look at issues of draw and ventilation, but I think just doing a comparison of

FTC and Health Canada would account -- the health Canada method would account for ventilation, and somewhat for draw; but looking at levels -- because that was the question that came up yesterday.

The issue of characterization came up, and I don't know the answer to that; but I think we need data. There are references to synthetic menthol compounds that are not characterizing, but have chemosensory effects, and is that something one should look at. If there are synthetic compounds that remove the characterization, but have chemosensory effects, could that be produced?

The effects of menthol, clinical. The chemosensory effects. I think they break into two areas. One is the thermal effects; and then the two effects, head and neck receptors. I would be very interested in behavioral research on that, as well as neurobiological research that included EEGs, MRIs, or other measurements of neurobiological activity.

I would be very interested in the interaction of menthol with those actual receptor

sites. Looking at issues of salivation, moisture.

I would look -- I would be very interested in neuroactivation. What is the level for neuroactivation to occur within receptor sites in the head and neck region? And how are those activations passed on to centers deeper in the brain?

I'm not going to be long, Jon.

I think the research -- we would be very interested in methods and in sampling. So that if we look at data supplied by the industry that we know, clearly, the methods and sampling, that if it's a qualitative or quantitative research, I think that would be very important.

Tied in with that is nicotine and menthol. We heard presentations this morning that there may be competition for -- I think the term "throat grab" was used. I would be very interested in not only thermal effects, but where nicotine and menthol become related in their activities. Any research where they're talking about both nicotine and menthol, particularly, nicotine and menthol ratios

within the rod, within the smoke.

Dr. Lauterbach referenced the interest, the concern about candy and flavor, and I agree with him; we should closely look at the issue of candy-like effects. I think what we also look at, is menthol irritating? Does it have an analgesic effect? Does it have an anesthetic effect? Does it have an impact effect? Does it effect smoothness? Does it affect amelioration? Again, that would be looking at tobacco industry documents relative to levels in the product. Are those effects varied by the amount of nicotine, which is delivered to the smoker?

Definitions of analgesia, anesthesia, and levels of smoke. Yesterday we researched data about dermal effects, but we did not receive data directly on the smoke effects on analgesic head and neck from menthol. I think that would be important to look at.

I'm almost done.

Smoke aerosol, deposition, and inflammation. I'm not sure how much information we

are going to get there. That probably gets back to the safety issue, but that's an area of interest.

I am intrigued, and I asked the question this morning about Menthol Crush. All of a sudden, we have got something new in the market where there can be the ability to manipulate dosing. If a drug manufacturer walked in and said, well, we can press the pill and we can alter our dose of Valium or whatever, I think there would be an enormous amount of concern. That has to be carefully looked at.

Are we treating this, you know, without sensitivity to human rights? So a product like Menthol Crush, I think that will be very interesting.

Now, marketing -- and I'm going to probably break that into three areas. Marketing. I would be very interested in trend data by subbrand for the unit sales and the price. And there are commercial data sources, it's my understanding. It's my understanding also that the marketing vendors -- the advertising firms for the agencies will be looking at age, race -- when I think of age

groupings, I would think of 18 to 25; 26 to 35; 36 on by subbrand. That could be data sources like Maxwell, Simmons, Nielsen and others.

Just to Melanie's point, there is a relationship -- I mean, there is a relationship between marketing terms and perception. I'm just going to read here, brand -- well, I will say it, Camel number nine.

DR. SAMET: Greg, you are in the process of redefining short.

DR. CONNOLLY: I am almost done.

This is the term that is used, light and lushes; lushes and aromatic with a touch of creamy menthol. This is a nicotine part.

Now, when we come to Camel Frost we have a different set of terms; infused with fine Asian menthol for an extremely cooling, crisp and clean taste. I would really like to see the marketing people that tested those terms among consumers.

I am going to end at that by saying, I think price discounting is also important, looking at price discounting by brand, by neighborhood, by

ethnic groups.

Thank you very much for bearing with me.

DR. SAMET: Okay. Thank you. You know, I think, actually the -- the -- perhaps the lengthening list should take us back to where we started, which is, how long does this report need to be and what evidence is essential to addressing the questions that -- at hand? Because, I think, clearly -- and by this passage around the table we have identified many topics. Some of public health relevance; some of scientific interest. And I think what we are going to have to do is refine this list probably after lunch. Think very carefully about exactly what we need in relationship to our -- our report. What depth of information we may need around, you know, particular issues.

So I appreciate Greg and everyone who raised all these points that they are all potentially relevant. I think what we're going to have to do is figure out what is most relevant and essential, in fact.

I think the other question that -- some of

the issues raised, there may well be -- I mean, I don't know -- but there may be -- for example, you were interested in some of the neuroresponses, and the extent of which sort of the techniques of neuroscientists have been brought to bear on these questions. Perhaps there are data that are in the peer review literature that simply did not come forth because of the nature of original searches. Some of this we may need to not only put into our industry request, but ask the FDA staff to explore as well.

So I think we should remember that, because we have that item of other information, you know, covered in one of our other questions.

Let's see, circling back. Ursula.

DR. BAUER: Yes, I was going to make a similar point, Jon, to the one that you just made. I would be most comfortable sticking close to the charge, given the short time frame that we have to produce a report and a set of recommendations. So looking specifically to what the statute is directing us to weigh in on, and identifying where

there are gaps in our knowledge, I think, will help us come to closure on the list of requests.

DR. SAMET: Yes.

DR. CLARK: I also would be interested in if the industry gave any consideration of alcohol and drugs use paired with menthol use, because we know epidemiologically in the populations when individuals have alcohol and drug problems and psychiatric problems, there is increased cigarette smoking. I'm not sure that menthol plays a role in that; but if we're asking them, they may realize that particularly in a high consuming population, these factors may play a role. So alcohol and drug use, and psychiatric comorbidity; like depression, anxiety, and stress.

DR. SAMET: Okay. Dr. Karol.

DR. KAROL: As part of the Indiana Health Service we have a fairly robust standard set for our people; and in a lot of the data that I have looked through this morning, having not been here yesterday, I don't see a lot of Native American data. So if there is something we might be able to

help with, because we have a robust RPMS system that does take down a lot of information about our population we might be able to get some of that up-to-date. Because my understanding was the Native American population have an awfully high rate of smoking and cigarette use. So that might be helpful and -- trying to remember what my second point was.

DR. SAMET: Is -- am I just likely to have brand -- cigarette brand information?

DR. KAROL: I don't know, you know. We have a fairly high smoke shop, and whether we can obtain that, I don't know; but it might be something we can look into.

DR. SAMET: Neal.

DR. BENOWITZ: I would like to see some information about international data on menthol. We -- it was my impression that the U.S. is the country that has the most use of sort of characterizing menthol brands. We heard about Japan. I don't know anything about menthol use in lower levels internationally.

So I really would like to get a

perspective of how menthol is used or not used internationally, because I think it would be informative. Menthol is not used at all in any way in most cigarettes around the world. So I would argue that -- if it's necessary at any level here. I have no idea.

DR. SAMET: I think some of the articles provided describe the use of mentholated cigarettes. I think in the Philippines and Cameroon, if I recall, perhaps, a few other countries. I don't think the article spoke specifically to your question.

DR. BENOWITZ: You know, particularly, any level of menthol which is used in cigarette manufacturing around the world.

DR. SAMET: Greg.

DR. CONNOLLY: Just add to that, I think geographically, I think that's of interest. Also, timelines. The modern cigarettes has been in America for 100 years. I would be curious 50 years ago what percent of the U.S. market; 30 years ago; 20 years ago; 10 years ago. So is this an

increasing problem? I think that raises complexities about initiation; but it, at least, provides a picture, you know, was the conventional cigarette -- did it need menthol to, you know, in essence, be the conventional cigarette? So timelines. Thank you.

DR. SAMET: Okay. Jack.

DR. HENNINGFIELD: A request that might be best by -- achieved by CDC or FDA, actually, is would it be possible to model with parameters that -- that maybe include ranges for the potential impact of menthol on initiation in populations on the basis of the studies that we looked at, extending cessation.

In other words, this, I think, goes to part of the heart of our charge, which is public health impact. So it's one thing to say it seems pretty clear that in some populations it's a contributor to initiation. Can we estimate the range of potential increase in smoking in young African Americans produced by menthol? And I am sure nobody can come up with the exact number; but

there must be some way of modeling what is projected on the basis of what we know about initiation, delayed cessation, or difficulty in cessation, you know, in at least some populations.

DR. SAMET: Okay. I think, clearly, the end impact might involve, at least quantitative -- if we were to get to the point of quantitative impact, it would involve modeling; and hoping that the literature would provide the values for parameters like you mentioned; risk, initiation, or effects or consequences for cessation.

So I think what we're going to do is we are going to stop for lunch. I think we have -- what we should do is after lunch come back and I think refine this lengthy, lengthy list. I think particularly given enough specificity that we can give guidance to the industry for the next meeting.

I guess I have to give the reminder. Do not talk about the meeting topic during lunch with yourselves, the press, or any member of the audience. So we will reconvene promptly at 1:00. Thanks.

(Whereupon, a lunch recess was taken and the proceedings subsequently reconvened.)

DR. SAMETH: Okay. I think we are back and ready to go. Miraculously while we were at lunch there was a refined list that was developed from our discussions before lunch. I think there is -- what's useful to see is that there were five different items listed out. I think, perhaps, reminding us that we do need to refine -- refine things.

So what we want to do is -- this is -- we're only right now addressing question one. We do have other questions that will probably be less time to address those. We're going to have a discussion, I think, brief one that Corinne is going to lead about subcommittee -- subgroup activity; and Neal needs to get a cab at 3:00.

Maybe -- is anybody else in that rough time domain to get to Dulles? Pretty much the same. Okay. So Ursula as well. Sounds like we're ending at 3:00.

So what I would suggest is that we go down

this list with an eye towards doing two things. One is deciding if the item is essential. Remember, this is essential to our meeting, our charge. And second is it, let's say, a first priority item. I mean, one that's -- that's information that we must -- that we must have. So some of this, I think, will be easy.

I think some of our items are probably redundant. We can just do a little bit of smoothing of text, I think, without doing a great deal of wordsmithing there, as long as the message is clear.

Cristi, I assume that after the meeting we can just sort of shape the text of the request without -- okay.

So I think I'm going to start, one to 35. So one. So that's our distribution of menthol. Mark.

DR. CLANTON: It's pretty clear some of these group quite nicely. So actually two through five, at least, and there may be some others that fit under marketing. So there seems to be a marketing category. There is a biomarker's

category, because there were several request for data around biomarker. So I just throw that out, because if we go through these individually we're still left with kind of figuring out, well, that's a marketing question; that's a marketing question. So some of them group together. Maybe we can throw those together pretty quickly; and then go through those groups.

DR. SAMETH: I think that's a helpful suggestion. Let me just say, I think we can all agree that number one is something we want, and we will -- we will put that as high priority.

And just if we were to take the category approach, the studies of perception; there is biomarker studies; there is marketing. We may have some other categories, and we can group as we go. Greg.

DR. CONNOLLY: I think for categories, I would think characterization of menthol, you know; that would be a whole group here. Effects of menthol. The effects would be both clinical effects, and, you know, including biomarkers,

chemosensory effects, marketing, and then population effects. I would think those areas are pretty much encompassing. You can categorize each one in those areas; characterization, effects, clinical effects, marketing, and then population.

DR. SAMETH: I have got the categories. I want to make sure within that we make sure and get at Neal's comments -- request for an understanding of the product itself; and it's manufacturing, which I think is your characterization.

All right. So let's -- I think we have got some suggestions. Let's try it out and see if we can get through this and get things moving.

Number one, whether it goes under characterization or whatever we can figure out, but we will like to stick with that.

Studies of -- let's see, so studies of perception -- these are your clinical areas. Greg, is that what you were -- marketing. Because I would actually say that a laboratory based study of perception is not marketing. That really --

DR. WAKEFIELD: Well, laboratory studies

are often used pretesting as a -- to help develop marketing techniques. So I think they are relevant.

DR. SAMETH: I think the relevant -- maybe we shouldn't be worried too much about lumping and splitting for the moment, because we can get caught in that. If we proceed in some logical order, let's stick with menthol and that end for the moment. So I think we had -- if we look at one -- I think is ten any different from one? I think this is all in relationship to menthol, but -- if I understand it correctly. Jack.

DR. HENNINGFIELD: Yes, I think it makes sense to have this one category whether it's characterization. Then it is, what is menthol? What is the dose? What do you put in? I think wherever possible, though, I think we want specific questions, as opposed to saying give us all of your studies in this area. We are not trying to get a truckload of studies.

DR. SAMETH: So under "characterization of menthol," if we start at the top of the list, I think going back to a presentation on the

manufacture -- the addition of menthol to cigarettes both -- I suppose in general and in mentholated cigarettes; and I think this relates back to the issues that Neal raised in terms of background for the Committee. So we put that under our characterization of menthol. So that's probably number one almost.

Beyond the content we want an understanding of the actual construction of cigarette -- the addition of menthol to the tobacco -- to the cigarette product. So that would come up under your characterization. I think here is where you wanted the studies of dose response for perception and sensory effects.

DR. CONNOLLY: I think under characterization -- maybe it's included -- but it would be by subbrand level, the level of nicotine in the rod, the level of nicotine in the smoke if it's available under ISO FTC and under Health Canada condition; and that would respond to your questions on filter efficiency and ventilation. That would be trend data. That would be looking at over time.

DR. SAMETH: Menthol content in the tobacco, and -- in the raw tobacco and in the smoke.

DR. CONNOLLY: And in the smoke under two conditions. One would be an FTC, and one would be an intensive Health Canada condition with blocking in a large population.

DR. SAMETH: If available.

DR. CONNOLLY: If available.

DR. SAMETH: Yes.

DR. CONNOLLY: That's something also the FTC could potentially subcontract to validate other research.

DR. SAMETH: Okay. Yes, Ursula.

DR. BAUER: I'm just concerned that we're going to ask for a bunch of information that potentially doesn't exist in the form that we asking for it. So if we are asking for studies that the industry has done on these various issues, maybe they haven't done those studies. Can we formulate those specific questions and ask for the industry to respond to those questions, which might involve not undertaking a formal study, but actually pulling

together information or creating information?

DR. SAMETH: Yes, let me ask -- Dan, perhaps, you can clarify this, and tell us -- give us some insight on what might be available.

DR. HECK: Yes, I haven't had the chance to consult with the representatives of the companies yet, but I have a sense from my own experience that there are large areas that we inquired about today that there is probably no information internally; but would -- no reason not to list it, I think. But let's not be surprised if there are not studies in some of these areas.

Again, I am not trying to play lawyer either, but if there are some areas of interest that tread close to trade secret formulas, that kind of information -- it might be that if there is a way to somehow consolidate that, and, you know, keep those appropriate trade secrets protected while giving you the information you need, that might be a way out of some of those circumstances.

DR. SAMETH: Yes, so I actually like the original route to this number one; and then

following, Greg, and if available, this more detailed information. Because we would take the information at its most general level that it may be available for the purpose of addressing our charge. So I think we should reinsert what was number one; and then the next sentence would be, if available. Greg.

DR. CONNOLLY: I do not think it would be an onerous task, or an extremely expensive task to contract with an independent laboratory to take the ten most popular menthol brands based on market share, and to do total rod testing, and then testing menthol and smoke under two smoking conditions if it's not available from the industry.

DR. SAMETH: Okay. So this may be something for follow-up, or for explanation, but we will -- I think we got number one roughly done. Number two had to do, I think, with this general call for information about menthol; so that would, I think, be number 12. Perhaps, 24 somehow fits in under there. And I think, 25, cigarette component, I think this is referring to particular gas phase

locations, where is it.

DR. CONNOLLY: I think I raised that, and that would be -- it would be going to Neal's question -- and you have already covered it -- where is the delivery? Is it delivered in the foil through -- is it delivered in the paper? Is it delivered in the filter? I think you have covered that already.

DR. SAMETH: I think, perhaps, what we should do is make number two, which I'm not quite sure I can interpret as it stands -- that would be a description of the manufacturing process and the inclusion of nicotine and the specifics of inclusion of nicotine within cigarettes. Is that fair?

DR. CONNOLLY: Yes.

DR. SAMETH: I'm sorry, I meant menthol. Thank you.

Yes, Jack.

DR. HENNINGFIELD: We are going through as though we need all this information. I think we really have to think about what information you actually need to determine if there is an adverse

public health effect; there is an effect on -- and there is an awful lot of information about menthol that we will love to know; but I think we really should give some thought about what is essential for us to do a report that's focused on the questions at hand, and not be --

DR. SAMETH: I completely agree. I think by the time we sort of refine our list, I think we need to go back, you know, as I mentioned, and decide what exactly is essential to our task.

Okay. So if we move down to clinical effects, this characterization of menthol content by cigarette component, this refers to the manufacturing. Might also refer -- if we need it, it might be a subbullet or something there saying -- back up under two, perhaps, of the sources of the nicotine; and the forms of -- sorry; I will try and stop saying "nicotine" -- menthol, that are -- hint, if I say nicotine, I don't mean it.

So if we put that there was question about sources of menthol and the content of the menthol that were being used.

Okay. And then down to the clinical effects. So that comes out; that's correct.

Then we were -- I think we wanted to know about the -- let's describe this. So we were interested -- there is a number of things here. Number 13 and 15 are somewhat the same. We are interested in dose-response relationship for sensory effects of menthol; and the extent to which there are data describing variation of those response curves by gender, ethnicity, and age. So that's 13 and 15.

Actually, 14, to me, is part of dose-response, whether the curve has a threshold. I think that takes care of 13 through 15. Those are under characterization.

I guess I'm turning to this next page, and there is this item 20, which I think, Greg, these were some of the things that you were talking about at the end, perhaps, some of the more elegant work that might or might not be available using more current techniques. Do we -- does that -- you want to move that up under our current categories, and we

can decide what priority to give that.

DR. CONNOLLY: Yes. So when we measure effect, we are looking at chemosensory effects, which would be a range of effects, including does it taste like chocolate to does it have impact? If there is neurobiological data, does it initiate action by receptor cites? And then, is there behavior research where people are measuring behaviorally in clinical trail -- clinical work, qualitative, quantitative perceptions of those effects?

DR. SAMETH: So in a sense you -- I mean, between numbers 27 and 20 -- almost getting at the -- and 30, these are actually studies of the mechanistic basis of menthol effects -- if it is fair to group them that way. Then there are a number of different ways you might go at it.

Yes, so this would be, I think, dose-response. So I think these would be mechanistic studies -- studies of the mechanisms by which menthol has effect, and those could include receptor interactions and other things. Dan.

DR. HECK: Mr. Chairman, may I offer this one suggestion as we get into this -- the request in this area. Some kind of nomenclature that would allow you to separate, you know, simple taste of reference tests, a focus group from, you know, a real thing would be useful.

DR. SAMETH: Okay. I think that's something we might refine as we go back through this.

Can we go just see where we are with this. I think we are not -- no, the other way.

All right. One, the characterization; we're done. Then, the next is clinical. We have the dose-response. Then I think that -- if I understand what we would like to put, number five would be the mechanistic -- mechanistic studies, which we may want to reframe with Dan's comments. The mechanistic studies of -- of menthol's effects, and that encompassed a number of things. Greg.

DR. CONNOLLY: I think number 30 could go in that category that you are looking at right now.

I would argue -- probably defer to Neal on

this -- should there be a separate, you know, question around menthol and nicotine, looking at research that -- looking at synergies or nicotine to menthol ratios. Should we keep that separate from looking at just straight chemosensory effects of menthol?

DR. BENOWITZ: I think that when we're talking about menthol, we're talking about menthol in the presence of nicotine; and so I think we have to.

DR. CONNOLLY: So it would be part of this, but maybe a separate category, menthol and nicotine?

DR. BENOWITZ: Yes.

DR. SAMETH: You would like to make that, perhaps, number six right now, studies directed at interactions of nicotine and menthol and numbers, ranging, dosing, and et cetera.

DR. BENOWITZ: I'm not sure what's available for metabolism. Certainly, a lot of things we heard about the effect of menthol on perception of nicotine strengths.

DR. SAMETH: Let's see, John.

DR. LAUTERBACH: I just had a clarification on Dr. Connolly's number one. Does he mean that would also include typical TPM, tar, nicotine, water, whatever on the smoke data, just the smoke menthol?

DR. CONNOLLY: Well, it would be nice to if you -- you know, if you did commission the laboratory to produce, you know, data in menthol, have to look at TPM, have to look at nicotine. In fairness, may want to report on ventilation, may want to report on draw. I think ISO, the Health Canada conditions with tar and nicotine reported gives you some really small area to look at that can provide insight.

DR. LAUTERBACH: Agreed.

DR. SAMETH: Dorothy.

DR. HATSUKAMI: Just related to what Neal was saying, I think it would be interesting, actually, to take a look at the effects of menthol on the harshness of tobacco products. I know we talked a lot about that. Whether that's related to

the nicotine or the tobacco smoke itself, I'm not really sure; but I think that that's a really critical area to determine what kind of effect menthol has on the perception of the harshness.

DR. SAMETH: So is there a need for -- under our current category, the clinical one on studies of menthol? I mean, I think this goes a little bit to Dan's point that the mechanistic studies might be quite different from effects of studies on menthol, on perception of smoke or response to smoke. So there is, perhaps, a -- perhaps, a broad body of studies there that may be relevant, correct?

DR. HECK: I do think, Mr. Chairman, that, you know, you have seen some of these typical taste evaluations. You know, they ask the test panel, do you perceive the menthol is just right? Is it too much? Too little? Is the tobacco taste too strong? Too light? Just right? They're fairly rudimentary.

I think to a large extent if that's responsive, you know, you will probably see a lot of those. If that's not what you really want, you

know, let -- clearly, set those aside. They can be considered separately.

DR. SAMETH: So Dorothy, is that a description of what you had in mind?

DR. HATSUKAMI: Yes, I think that's how --

DR. SAMETH: Melanie.

DR. WAKEFIELD: I think the difficulty in this area, taste is so intimately tied to something. I think things like smoothness and harshness and strength are perceived after inhaling, as well as before even lighting up in terms of expectations being created. So I think the taste information is really important, because it's all about false beliefs, I think.

DR. SAMETH: Let's make sure we got this prescribed. We are interested in studies of smokers' perception of -- I guess, taste is one. It's really smokers' perception on whatever parameters have been studied of smoke for menthol and nonmenthol cigarettes.

DR. WAKEFIELD: I think it's studies of attributes of the cigarettes and of the inhaled

smoke that are intimately related to perceptions of harm of the cigarettes. And those perceptions might be framed in terms of smoothness, strength, harshness; as well as direct perceptions of harm or protection from harm.

DR. SAMETH: So it's studies of consumer perceptions of smoke and of the harm of the smoke is what you are saying?

DR. WAKEFIELD: Yes, of the cigarettes themselves before they're smoked; and of the inhaled smoke after it's smoked -- after it's smoked.

DR. SAMETH: Okay. Neal.

DR. BENOWITZ: To follow-up on the conversation about the machine testing. One thing that's come up at this meeting, and which I thought was interesting, is that potential different relationship between menthol versus nicotine and tar deliveries based on the kind of cigarettes. So it sounds like with the lower dose, menthol can be used as a substitute; or nicotine, perhaps, is lower because you are having another substance that's causing a throat response.

My impression, look at menthol, characterizing taste cigarettes. Most of them are higher in nicotine and tar than cigarettes that are not menthol characterizing. So what I would like to do is have an exploration of those two kinds of cigarettes in relationship to nicotine and tar. See if we're looking at two kinds of worlds of menthol effect and tar exposure. Is that clear?

DR. SAMETH: In a sense. I guess the question is whether we have covered that in our prior points about interactions of nicotine and menthol.

DR. BENOWITZ: I just want to make sure we do a specific analysis within the two types of cigarettes. So the low menthol cigarettes, and then the menthol characterizing flavor cigarettes, and the relationship between menthol delivery and nicotine and tar.

DR. SAMETH: So one possibility is that we weigh what we hear in response to more general questions, and see if there is potential to explore that question. Think about what might be essential.

Greg.

DR. CONNOLLY: Before you get back to Dan's point, is that we are looking at a number of attributes that may be affected by the different dose. I think we heard testimony -- or we heard presentations yesterday that referenced that, perhaps, a low level nicotine may create feelings of smoothness; or a higher level of nicotine creates a smoothing effect or almost analgesic effect. I think that we heard yesterday there are thermal effects, and there are nonthermal effects.

And to what Melanie said, the definitions will probably vary between companies, but thermal effects, analgesic, and anesthetic effects. Nonthermal effects would be irritation, smoothness, impact. General areas you can add to that, strength, amelioration and others. I think it's differentiating thermal, nonthermal.

Then, trying to wrestle with the issue of dose and population. We did hear data on that yesterday. There may be a relationship with low dose and younger smokers. There may be a

correlation between high dose and smokers. I think that information would be helpful.

DR. SAMETH: Jack.

DR. HENNINGFIELD: Part of the difficulty we're having is because we don't know what universe is out there. And I think we are going to have to trust, to some degree, the uptake of what we're looking for; discuss with the companies what they have. Maybe they will have to come back.

As I see this, we're looking in this area -- two categories of study-related information. One is from the focus group type panels that are giving them whatever attributes they use. We're guessing whether smoothness, harshness. I don't think we should be too specific, should have examples. For example, smoothness and harshness that are probably translated in marketing.

Then, we also need the kind of data that I assume are more laboratory data on the dose response. Because the industry has to have some basis for knowing how many grams to put in and how many grams to put in what; and what is the threshold

for what. I don't even know what responses are used to determine a threshold; but how do they figure out how many milligrams should be put in. That, you know, a lower content versus a characterizing one. There must be dose-response data on that. And I don't know what's that for.

DR. SAMETH: So two comments. I think your point about examples is important. We might specify, for example, studies involving.

I guess the other question that maybe we can pose to Corinne, there is, you know, then -- I think we would want FDA to provide a list specific as possible to which a reasonable person looking at it would say oh, this is what they're after.

I guess the question is whether there would be give and take. The industry responds to the issue, perhaps -- do not know what to anticipate; or do you have some ideas from any discussions already about how this process might unfold?

DR. HUSTEN: I think the question before you right now is what you would like the industry to

present at the next meeting, which, you know, we hope will be in the summer time; and so I suspect if these are the questions you want industry to respond to, we will put that forward.

DR. SAMETH: And I would say in a reasonable process if there is ambiguity, I would hope that the industry would come back and say, can this be clarified, so we are efficient in our task. We have a timetable. It would be unfortunate at our next meeting because of any doubts as to what we wanted, we don't get what we think we need as of today.

So I think it's really a request that we receive back what it appears that we wanted. If there are questions about it, that we hopefully can have those clarified.

DR. HENNINGFIELD: Can I clarify something on that, because the FDA also has experience with where you get into trade secrets. We don't necessarily have to have the trade secret data. And so if the industry says we can't give you this because it's trade secrecy that has recommendations,

FDA has mechanism for getting information that the Committee needs without divulging trade secrets. I would assume that's something you folks handle, meaning FDA.

DR. HUSTEN: There is information being provided to the Committee, you know, as part of standard FDA confidentiality work of CTP.

DR. CLANTON: One of our requests -- I want to make a point. There may be a lot of softer data as it relates to consumer preference. I will say if we want perception data, more laboratory based, we need to ask separately for that. I want to make the point that we do want information and data around preference, which is at that very simply level of individual sit down and make a decision that they want one thing over another. I think we do want to see maybe softer, less scientific marketing data around preference; and make it clear that preference is different than perception, at least as studied by chemoreceptors, that type of thing. We do want studies that are marketing and consumer oriented.

DR. SAMETH: John.

DR. LAUTERBACH: Okay. Couple points. We have been dancing around this point subliminal menthol. To give you a comparison, in one of Dr. Heck's health inhalation studies he had menthol levels 5,000 PPM. A particular subliminal might be 100PPM, which does present analytical laboratory looking for that; somewhat of a challenge. Not impossible, but can be done.

Secondly, when sensory work is generally done in the tobacco industry, most of the time, not always, is done with nicely conditioned, well-characterized cigarettes. And moisture can be a tremendous reducer of smoke harshness. Just having a moist fully conditioned cigarette versus one left on the dashboard in the open desert can be a tremendous difference in harshness.

DR. SAMETH: Okay. Dan, I think you are next.

DR. HECK: I was going to offer an earlier clarification. I would ask -- I think the discussion with the FDA will help us clarify what is

needed for my own understanding. I would ask -- for the Committee's understanding, know that we have some deadlines here. We also have some harsh deadlines here. I would ask that we try to refine in discussion our must have needs distinguished from the, you know, might be nice, and indeed from the newly created data suggestions we have, which would probably take months to initiate and months to complete.

DR. SAMETH: I agree. We need to stick with what's essential.

DR. HUSTEN: I just want to say it's important for you to be as clear as possible with us about the questions you want asked. While we may be able to do a little bit of administrative follow-up, you know, the question can't be offline. We need you to be clear so that we're not trying to interpret what we think you said you are telling us what you want.

DR. SAMETH: Got it. I think -- Ursula.

DR. BAUER: Yes. I think more of the same point. When I get a data request -- and I get a lot

of them -- it's much easier to provide the most relevant information when I understand how the data is being used, what the purpose of the request is. We want to be clear that we're asking for things that help us answer the specific questions we have been charged to answer. Even though this is an opportunity to get a ton of information, I think we do need to be very focused.

DR. SAMETH: Dan.

DR. HECK: Just a real quick hunch. My sense of the volumes of such studies -- I haven't talked to represented parties -- there is probably 98 typical case study surveys. Of those, one or two more science academic type studies. So that's my sense.

DR. SAMETH: Okay. I'm going to suggest that we move on into another category, moving out of clinical category. I would say maybe one thing, go under clinical, separate or biomarker studies. I do think we probably need to see and -- whether that goes under the clinical studies. We want to create a biomarker category. Why don't we do that for now.

So both. The biomarker category we can just say under that I think we are interested in laboratory or population studies of biomarkers in relationship to menthol content. Is that a fair -- of the cigarettes? Okay.

Dorothy, you agree with that? Okay.

DR. BENOWITZ: John, I wanted to ask one thing we haven't really dealt with is differential risk by differential numbers of cigarettes smoked per day. I would like analysis to include by cigarettes per day.

DR. SAMETH: John. False alarm.

Why don't we move to marketing. I think we are here. We have -- we have consumer reference data. I think there was a fair amount of studying 31, 32, targeted marketing to specific population groups. So the consumer preference data fits there, and then the targeted marketing.

So the old number 6 is why does the industry make menthol cigarettes? I am not sure exactly where that fits in. Perhaps, local --

DR. CONNOLLY: I would say

characterization.

DR. SAMETH: Characterization. Maybe the answer to that question almost comes out of characterization; almost a substatement.

Okay. Let's see. Go down to marketing, consumer preference data. Consumer perception studies; marketing of new products; marketing products by -- that's brand and subbrand? Melanie.

DR. WAKEFIELD: So marketing is pretty broad. So maybe we want to be a bit more specific here and ask marketing expenditures for the top ten menthol brands by time, something like that.

DR. SAMET: I'm not sure the right way to ask this. We do want to know if there are existing marketing strategies and their nature. Then you may also want to have additional information as to expense. Is that fair?

DR. WAKEFIELD: I think that would be helpful, because we have seen some trend data over time in terms of consumption and preferences; and that might be helpful to unpack some of those trends.

DR. SAMET: And probably -- maybe that "A" is a "B;" and the "A" is -- the question is the existence and nature of any targeted marketing strategies. Jack.

DR. HENNINGFIELD: Maybe help the FDA -- we help to, I think, make it clear what we're looking -- you know, what we're looking for. We're not trying to do a marketing report, per se; but we are looking at people -- of evaluating the public health harm and what goes into that. And what goes into that is what expands the market? What kinds of things are done to grow the -- the category? And whether that includes recruiting new smokers that were not formally smokers; retaining people that might have left smoking all together; promoting relapse.

Anything -- I mean, any consumer marketer has some idea of what kind of people they're going to bring into grow the category and expand their market share. And so there has got to be information on that; but that's what we're really looking for, whatever increases the numbers and

keeps more people in the market.

DR. SAMET: Okay. Greg.

DR. CONNOLLY: I think basic to marketing on 12 is just knowing unit sales by subbrand over time; and if data is available by gender, race, and age, that would help. I think unit sales are really the basis of that. We're looking at trends of brands where we know menthol levels.

And the second -- this is to Melanie's point -- is the advertising. And what I was hearing yesterday, seems to have shifted from advertising of cognitive messages many years ago -- you know, this is going to be safer for you if you smoke menthol back in the '30's -- to more advertising of effects.

And I read to you just from two different brands, one with low nicotine where the term "smoothness" was used. And then another brand in the advertising terminology described "vogue." Those terms -- has there been research to base the use of those terms among consumers that relate to the consumer perceptions of effects? I hope I'm being clear.

I know advertising firms will do qualitative research around products looking -- it could be ketchup -- looking at, is this ketchup smoother, or is this ketchup stronger? It would be nice to have that type of data, or that qualitative research.

DR. SAMET: I think we probably have that captured now between 13 and 14. I think the question of the sensuality of what you discussed is something that we will have to address.

Just to keep us moving, in terms of our categories, the one we haven't dealt -- looked at yet is the population effects. So let's take a look. I'm not sure we were -- so there we have, in a sense, the 22, post-marketing surveillance. I'm going to -- Neal, your international menthol data question, I'm not sure where it fits; but if we can could put it here for right now or somewhere.

DR. BENOWITZ: Or characterization.

DR. SAMET: Or characterization. So that maybe goes back up there. Why don't we scan our list. Karen.

MS. DeLEEUW: Yes. I think this goes under population effects, but I brought up the question of any information that might be available regarding the notion of switching from menthol to nonmenthol cigarettes. And I think it gets directly to the second point we're being asked to address in the report, which is the increases or decreased likelihood that existing users of tobacco products -- and I'm assuming we're talking menthol cigarettes -- will stop using such products. It seems to me that if the tobacco industry knows this is going on, they must be planning on something happening.

And the question I have is if -- is if banning menthol cigarettes will cause a number of people or will then be another factor in supporting people to make a quit attempt, then I think it's imperative that we know that information. And that information, I think, on a population level will be very useful to us.

DR. SAMET: So are there two items that we want within your question? One is -- what is up

here now -- quantitative data around the rate of switching from menthol to nonmenthol. Then, another, again, at the population level, the rate of cessation among menthol smokers versus nonmenthol smokers. Is that --

MS. DeLEEUW: I would say primarily the first.

DR. SAMET: The first. Do we also think -- we certainly need the second for our impact assessment.

MS. DeLEEUW: Yes.

DR. SAMET: Greg.

DR. CONNOLLY: I think to Neal's point, an international -- I reference the Japanese experience, which I, quite frankly, am not an expert on, and I was trying to draw it from experts. But I think the international experience for countries that haven't had menthol, and that we see a surge in menthol, that's a population effect. And I think how that happened -- how the industry -- how the industry participated or effected, then, that's a very nice interest.

The second is both to Karen's point, your point, Jon, is I think we should keep thinking subbrands, subbrands, subbrands. Is there variation unrelaxed by subbrand? Is there variation initiation by subbrand? Because a subbrand hopefully will have knowledge of level.

DR. SAMET: Okay. Dan.

DR. HECK: I had a residual comment from some of the earlier discussion, but we have to recall that as we tread close to the marketing and trade and business elements of the business, the industry has, as you know, severe antitrust constraints on our ability to coordinate among ourselves in terms of even answering your questions. So we would -- we would have, you know, independent answers from every company who may have slightly different internal nomenclature or perspectives. What we can do up front to try to make the data such as may be turned over and understand what -- I think it will be worth the while to work up front with FDA and the Committee.

DR. SAMET: So I wonder if we could go

back -- I think we may want to decide that we want more on the population. If we go back up to the top, let's do that. And let's now both look at these and make sure we have said what we wanted to say; and then at least identify those items that we view as the highest priority and necessary for meeting our charge in developing this report.

So number one, menthol content by brand; all types of cigarettes changes over time. Then this additional elaboration that Greg proposed. So I think -- essential. Okay.

So number two in a sense is background, qualitative description of industry understanding of menthol, description of processes. This is probably essential background for our report. So we will star that.

Okay. Three. Essential.

Okay. Four, this is a matter both of historical precedent, not only do cigarettes go back a long way, possibly motivations have changed over time. Is it helpful or essential to our charge to have an answer to that question? I think we can --

okay, I think I am getting a sense that this is certainly not as high as others. Let's just leave that one unstarred.

Is there a counteropinion? Greg.

DR. CONNOLLY: It's not counter. If a drug manufacturer presents before an FDA Committee, I mean, intent is critical element to the -- of, you know, looking at a medical device or products. So that's an intent question. What is the intent of menthol? It could be simple; I just want to add chocolate or make it taste like chocolate. It could be more of a complex response. Tied in with that, I think it's important. Is it essential? Do we deem it to be essential to a conventional cigarette? I think intent -- I think it's a question of intent. I think it's important.

DR. SAMET: So it's half masters.

DR. CONNOLLY: Yes.

DR. SAMET: Jack.

DR. HENNINGFIELD: A number of people in this Center are from CEDAR, and presumably they need more help at CEDAR; but some of these -- whether

it's intent, justification, but routinely a drug manufacturer may be asked about the design or an ingredient as to how to justify it.

Particularly, whether it is the possibility that that might add harm. So I think what we are asking here is analogous. There is -- menthol carries whatever name risk in certain areas; how is it justified? If it can't be justified, why would you allow it? I think it's in the industry best interest to provide whatever intent, benefit, justification, because that's what we're looking for.

DR. SAMET: Okay. Ursula.

DR. BAUER: And just to clarify, when we're asking if menthol is essential we're talking about menthol in all cigarettes, not just mentholated cigarettes.

DR. HENNINGFIELD: I think both, because, again, why would you put it in if it contains potential risks at levels that people can't, obviously, detect it. If there is no good reason for it, why should it be allowed?

DR. BAUER: Our charge is to try to evaluate that risk. How are we going to do that?

DR. HENNINGFIELD: I think this is independent of the risk. We are just finding out why, and what is the justification. Why do we have testimony today about the -- you know, from two -- public testimony from two companies basically are doing the menthol should be left alone. What is the justification?

DR. SAMET: Let me pose a comment and say that I think this is nonessential. It is there, and our charge relates to the impact of it's being there, regardless of whether it's there for flavoring, sensory perceptions, or anything else. I am just not sure that this is an avenue that's going to lead us fruitfully towards our charge. I'm not sure -- let's leave this without asterisk for the moment, and move on down to clinical effects.

And actually, here is probably an example of one where if we added an example, for example, studies involving, it would probably be useful.

Let me ask Cristi. Could we, after the

meeting, fill that kind of detail in, you know. Say here, for example, studies involving smoking cigarettes with varying menthol content and assessment of perceptions of taste. I mean, could we --

We want to fill it in a public form.

Okay. Let me make a suggestion that we continue our work, then, decide if we have time to fill this in, in public. If somebody while you are sitting here in public wants to jot down some examples, then we can add them back in, that might speed us alone. For example, Jack I, I suspect you can do that or others. So if you all would like to think about specific examples that we can add in, then we will circle back and add those -- add those in.

Dose response, I think an asterisk here for sure.

Now, the mechanistic studies, which is potentially broad in range. Where does this fit in our priorities? This nods for essential. Okay. So we give asterisk there.

I think seven, I think we can agree is essential, without question.

And eight is also essential. We are on a roll.

Marketing data. Consumer preference data. Yes.

And ten; yes, I assume.

Let's discuss 11 enough to know if this -- what we would want, and is this essential?

So, Greg, I know you brought up Marlboro Crush, is this essential?

DR. CONNOLLY: I don't think it's essential.

DR. SAMET: Okay. So not essential.

Then 12 is essential in both of its components.

Thirteen. Essential. Okay. So that's an asterisk.

Okay. Fourteen. So there was a substantial amount of discussion related to descriptors and how they were used in their consequences. It actually seems to me we have

almost got that same kind of stuff under other bullets. This is a specific thing.

DR. WAKEFIELD: It is. It is probably more of an example. I think it's kind of subsumed under the others -- one of the earlier points.

DR. SAMET: Where would you like to move it? Let's just for the sake of simplicity, move it up.

DR. WAKEFIELD: I think it's about 12.

DR. SAMET: Marketing.

DR. WAKEFIELD: Isn't it ten?

DR. SAMET: Okay. Okay. So keep going down. Biomarker studies. So 14 and 15 is really a subcategory of 14, I think. We just might say "including." Okay. That's essential.

Okay. And then population effects. So 15 is a yes. And 16.

DR. CONNOLLY: I think I did recommend that we use the term "by subbrand."

DR. SAMET: What I suggest if we say "by subbrand," we say "as available." Patricia.

DR. NEZ HENDERSON: I think it's important

that we include the differences in subpopulations too as we are doing this.

DR. SAMET: So again, we could say as available by subbrand and population group. Okay. I think that's true for 15 and 16. Okay.

DR. BAUER: Is 16 something we think the industry can provide to us, or does that go under our question two, which is what other information do we need?

DR. SAMET: Well, if industry could provide the data we would certainly be interested. Whether such data exist, we don't know. I suppose we can ask and find out if they are available. Certainly interested in the general question. I don't know if industry harbors such data. If they did, we would be -- we would be interested. I have no idea.

So should we leave 15 and 16 and put asterisks on them? The answer may be no such data are available, but we will have asked.

Greg.

DR. CONNOLLY: We have used the term

"switching." We have used the term "cessation." Just in recognition of the statute, have we put the term "initiation" in on 14 -- no, under population effects we talked switching, cessation. Maybe 15 becomes switching, and then -- "A" is switching; "B" is cessation; and "C" is initiation.

DR. SAMET: What you are then asking for is quantitative data around the comparative rates of initiation, switching, and cessation. So there is essentially one question with three components.

DR. CONNOLLY: Right. Let me say, even if we know use by age, like 18 through 25, by unit sales, trends; that's good information to have. We asked yesterday Ralph Caraballo on a number of occasions about brand specific data by age. He stated it wasn't available. And so if it is available by age -- legal age, 18 through 25, that could be helpful.

DR. SAMET: Okay. So the -- at the population level what we're asking for is, again, information on comparative rates for menthol versus nonmenthol cigarettes of first use and initiation of

regular smoking; switching, which is not actually a comparative issue. That's really switching from -- I guess, could be by directional, but we're interested in the nonmenthol to menthol switch. And then the comparative rates of cessation. Okay.

All right. Then I saw post-marketing surveillance down there actually. I think this is all encompassed. And we moved international up.

I think 17 is really in a sense our determination, I would think. I mean, is there something that someone would think of requesting in terms of from the industry, a presentation in relationship to -- between 15 and 16. I think I would take that off. Patricia. Jack.

DR. HENNINGFIELD: I think it's already covered.

DR. SAMET: I think we can just delete that. Maybe we skip down. I think we have probably -- is there anything left. Is it just the 16, 17. Oh, okay, there is more. Oh, no.

Where is the delete key?

Okay. So getting back to sort of

essential, nonessential points. Sixteen.

DR. WAKEFIELD: That's a conclusion we have to draw.

DR. SAMET: Okay. So 16 can be taken deleted. Seventeen.

DR. CONNOLLY: I think that's covered.

DR. SAMET: I think we have covered that.

Patricia, you had proposed number 16. That is something that can be moved up under the products -- in terms of the first very first category characterization, I think. Is it essential?

DR. NEZ HENDERSON: Yes.

DR. SAMET: Okay. Essential.

Could I ask our industry representatives on this point, is there likely to be a source of data, or how would this be obtained?

DR. LAUTERBACH: I will attempt to get some of the data. I can't make any promises.

DR. SAMET: Okay. Thank you. I'm not sure I know what 17 is, but I think we can probably take that off. I think we have got that.

Okay. Neal, I think the current 17 was yours. Have we -- have we covered -- will we have covered that in what we have put adequately above?

DR. BENOWITZ: I think so.

DR. SAMET: And I think we have subsumed 17 under our marketing -- yeah. Yeah.

Okay. Now, 18, we have not yet addressed. It is sort of an other consideration. Here, we would be looking for -- as stated, I don't think it's -- it's answerable. I mean I think -- and Dr. Clark is not here. Would somebody like to take a crack at thinking about what this might be in terms of understanding of combined drug use is the question, whether menthol compared with nonmenthol cigarette users are at greater risk for alcohol or drug use, or there is combinations interactions that are important I think from a public health point of view I can understand there may be an important issue buried here, but I'm not sure I can quite pull it out, though. It may not be an industry issue.

DR. CONNOLLY: Yes, I agree with you. I don't think it is an industry issue. There may be

better data sources that Dr. Clark can provide.

DR. SAMET: So, perhaps, when we come to other issues -- you know, for example, is there differential uptake of menthol versus nonmenthol cigarettes by persons with psychiatric disorders or with drug and alcohol problems. I mean, I think there might be some questions that can be framed that are public health relevant. Then 18, I think we -- the international we have right. It's gone up, right?

Corinne.

DR. HUSTEN: Since there are -- I'm not sure how many questions we ended up with -- 16 questions. We had planned on a meeting in the summer, you know, largely devoted to industry presentations; but there is a lot of questions here. I am wondering if it's -- it's seeming to me like we might need more than one meeting for industry to present on all these questions.

Perhaps, you could get -- maybe make a secondary prioritization of which ones you would like in the summer meeting versus the meeting after

that, whenever it is held. Because I'm not sure it can be covered in a single meeting.

Then, the other questions I have is whether our industry representatives, perhaps, could coordinate at least whether its nonproprietary data on the presentations, so it is not, you know, each company repeating the exact same information.

MR. HAMM: I think that's a worthy idea.

DR. SAMET: Okay. Neal.

DR. BENOWITZ: If we do that, I would raise the suggestion that we talk about characterization and mechanism in the first one; and then marketing and population in the second meeting, because it makes since to lump it in that way.

DR. SAMET: Dan.

DR. HECK: I think that also makes sense, because no doubt the business related things would be the more troublesome things to -- of a more competitive nature.

Again, I have the sense, and I will get the best information from the represented parties. Perhaps, 80 percent of these questions there will

not be data at all. I can refine that sense as soon as I can. But I think it's just a fact that there won't be.

DR. SAMET: Okay. Corinne.

DR. HUSTEN: I was going to say, I guess if you could give us that sense, then, we can make a determination, you know, is it feasible to do this in the next meeting, or should we plan on two different meetings?

DR. HECK: I would be happy to.

DR. SAMET: I think Neal made a very reasonable proposal for what would be sort of what might come first, and what might come second. I think it would be useful to get sort of a delivery of all the information related to characterization, and not have it come in, in two meetings, for example. Because at some point we're going to have to get down to our direct task. We could gather evidence for too long here, I think.

So why don't we leave this for the moment. Before we get to 2:45, which is not to far away, it would be nice to revisit with a -- to insert a few

specific examples of studies. So for those of you -- for example, think about marketing, et cetera, et cetera, if you could have a few examples ready to read out when we make one last past through, that would be helpful.

So I think we have gotten question one done.

Now, question two, so sweeping as to not -- not quite the fine answer. What other information does the Committee need in order to meet its statutory requirement? And I think we should think about this with an eye to what sources of information we may want the FDA to begin to develop, perhaps, in collaboration with CDC and other agencies. And I am going to make a specific proposal even approaching, perhaps, some of those people who are carrying out epidemiologic studies that might also be relevant.

I think, here, again, we should be thinking time limited what we should get, which is probably not to the published literature; or in expanded literature reviews, that might also be

useful. So let's open this up for a few minutes of discussion. Jack.

DR. HENNINGFIELD: With the caveat that what I'm asking for we can only approximate is some kind of model based on projections of initiation perpetuating use by undermining sensation, increasing dependence. These are areas that we heard that there are studies on. And they are areas that, I think -- it is a good case in point where you just don't average all of the data and say there is no effect. You look at studies that do show a strong effect in one population and come up with some kind of modeling to give us an idea of the range that is hopefully more than just directional.

And by the range I mean, what is the increased potential number of smokers because of the use of menthol and marketing? How many years -- are some people smoking longer because of menthol, and so forth?

DR. SAMET: So I think there is -- probably the issue could be, what models are potentially available? I think, you know, the sort

of range we have, the work that Ken Warner and David Mendez has done; David Levy, and SimSmoke; the work done by my former Hopkins group, and others. I think the question would be, what models exist? Have any been used to address issues related to menthol? And what might be useful for modeling related to our charge? If that's a fair statement, Jack I, I think I know where you are heading.

DR. HENNINGFIELD: It is. I think this public transparent process, frankly, facilitates that. Then they can be presented in open session. People will disagree over the parameters, but at least then the world can come to some idea as to what the direction is, and what the magnitude might plausibly be. That would be helpful to our charge.

DR. SAMET: I agree in terms of meeting the charge as it relates to impact. The availability of such tools would be extremely valuable. Neal.

DR. BENOWITZ: There were two areas that we heard about yesterday where, I think, there may be some additional data we could hear about.

Epidemiology was one. I think that Ralph actually said there was some unpublished data that he has. Others may as well.

I think we really do need more about temporal trends, about transitions. So if we could have access to either additional analyses from CDC, or at least unpublished data from CDC that they worked on, that would be helpful.

DR. SAMET: More detailed analysis than some of the survey data presented yesterday.

DR. BENOWITZ: Yes. And if there are other databases that could be looked at, because I think Ralph said there were several databases that have not been analyzed in this way.

The second area where there was a lot of uncertainty, at least in my mind, was with dependence, quitting, relapse; and there has been a fair amount done. I know one group, Dr. Okuyemi has done quite a bit, and his group; a bunch there with African Americans, in particular, which is the biggest concentration of menthol. It might be worthwhile to invite him or someone who has been

working in the area to really try to do a more thorough updated review of just these specific questions about dependence measures, quitting, and relapse.

DR. SAMET: Perhaps not at this meeting, but at future meetings as we shape the agenda. Okay. Let's see.

DR. HUSTEN: Jonathan.

DR. SAMET: Clarifying?

DR. HUSTEN: No.

DR. SAMET: Okay.

DR. LAUTERBACH: Just one thing on additional information that, I guess, the FDA staff needs to be aware of, because it's not indexed in Pub Med or anything. There is a set of volumes called "Recent Advances in Tobacco Science." And in 1993 a lot of the questions -- there was a whole symposium on menthol. And a lot of the questions that came up here, at least as of 1993, the answers to were in this book, okay. And these are available from the library of Crop Science at North Carolina State University. So there is a whole series of

these things that could be of use -- that should be included in the literature searches done by the FDA folks and CDC.

DR. SAMET: Okay. Thank you. It would be helpful if you got the specifics of these and other volumes; it would be helpful. Thank you, John.

Okay. Corinne.

DR. HUSTEN: Could I just ask Neal a clarifying question. You talked about additional epi studies. There was a lot of epi data presented. You talked about temporal trends and transitions and more detailed analyses and use of other databases. Can you be a little more specific about the specific questions you would like further analysis on, because Ralph, obviously, has presented a wide range of things.

DR. BENOWITZ: Well, the most important question is sort of what happens between the cross-sectional picture of adolescents, which had a certain fairly high prevalence of menthol smoking versus adults, where it was lower. So is this switching, or is this a cohort affect? I think

that's a very important question.

The other issue -- and I don't know whether it's available, but it would be very nice if there was some data to answer the question, if you initiate with menthol are you more or less likely to become an adult addicted smoker?

DR. SAMET: Actually, just to clarify Neal's comment, I was going to propose -- and I think this is probably something that staff could and should get started on -- is if you query the major epidemiological studies that are longitudinal, some by -- started by NCI, some by NHLBI, some by other agencies that have collected information in some cases on smoking among children, adolescents, and young adults -- the CARDIA study, which was mentioned yesterday, is one example.

In cancer there is a cohort consortium that involves most of the major cohort studies around the world. I think the question is while they probably certainly all have information on cigarette smoking, the question is whether any of them have collected information on menthol. For

example, the Nurse's Health Study. I simply don't know, but I think it would be worth a standard query to the principal investigators of all these major studies.

MSA, which is, you know, a major cardiovascular disease study. All the sort of the whole family of studies.

I think what we would ask you to do is to find some way to obtain a listing of those studies, and then ask systematic. This may be information that would be useful. There may be information on changes in cigarette use over time; and then the epidemiological questions of risk as well; but may not be any data there. Greg.

DR. CONNOLLY: You know, we have talked about models; and then talked about looked like secondary analysis of existing data sets. I would encourage FDA to commission research; and the -- could look at smoke chemistry. There is no reason why they couldn't commission laboratories to do independent research on smoke chemistry or raw chemistry. Clinical effects. I don't know what the

world looks like out there, but can -- you know, can researchers be approached, you know, within the constraints. I realize we're dealing with constraints here.

I think yesterday we were looking at a lot of research where menthol may have an add on to that study, and wasn't directly looked at.

CDC presented data yesterday on qualitative research, almost borderline focus group research on perceptions of messaging. Could we see that repeated by groups that, you know, conduct focus group research, and will consider it as such? I would encourage FDA to creatively think about going out and for every question we have asked the industry, think is it possible to go in and either find secondary analysis of existing data or if you have to go out and contract to have that data -- have these questions answered by new data.

DR. SAMET: Within a year or less.

DR. HUSTEN: Yes. To that question, certainly primary data collection would require us going through the OMB process; and therefore, the

time constraints may not allow that. We can check, but that's a six month process before you even get permission to start the study -- at least a six month process.

DR. SAMET: Ursula.

DR. BAUER: Yes. Just along the same lines, if FDA could put out a call to the field to look at ongoing studies and see if some of these questions can be answered. I know the New York State Department of Health has two long-term cohort studies going. One of youth at risk for becoming smokers; and one of adult smokers and recent quitters, both designed to look at transition; and there may be a number of other studies like that where a quick analysis of the existing data could answer some of these questions.

DR. HUSTEN: I think that's potentially more feasible.

DR. SAMET: Dorothy.

DR. HATSUKAMI: One of the potential adverse effects from menthol cigarettes is the possibility that they may not be as responsive to

pharmacological treatment. And that was shown in the slide that Dr. Hoffman presented of Dr. Okuyemi's study where people that were administered bupropion did less well when they were smoking menthol cigarettes.

So I guess I'm curious to know whether there might be some other data sets that might be used to do that kind of further analysis of that particular area, determining whether menthol smokers do respond less to -- or not as well to pharmacological treatment than nonsmokers.

DR. SAMET: Some of you may -- some of you know a lot more about this than I. Was information on menthol included in some of the critical -- major clinical trials, for example? And could that be pursued as a modified response?

DR. HATSUKAMI: That's a good question. There have been a number of clinical trials that have been conducted. If they asked about brand of cigarettes, that's a possibility.

DR. HECK: To your comment on the Okuyemi study and bupropion, it may very well be worth

pursuing. It is an interesting observation. I do recall from those studies menthol was also evaluated in the placebo groups; and the significance was lost. So in terms of evidence for menthol as an independent factor it seems to be less prominent in the placebo groups.

DR. SAMET: So what would be useful would be just to simply try to look at the totality of evidence in my view that might be relevant. Karen -- let's see, Patricia.

DR. NEZ HENDERSON: I would be interested to look at the questions that we propose to the industry for -- maybe for UCSF to look at these questions as well, because they have access to tobacco industry documents. There may be information in there that we might be able to use.

DR. SAMET: I guess the question would be do we -- are there targeted searches that we would ask that FDA staff, perhaps, in collaboration with the library facility at UCSF carry out?

DR. NEZ HENDERSON: Yes.

DR. SAMET: Okay. This may be something

for future meetings, in fact, an agenda item. Corinne.

DR. HUSTEN: Yes, I was going to ask, again, if you had a specific question that you wanted to specifically -- to try to get those analyses done. Because, again, if there is 16 questions, I don't know how quickly we can get 16 questions searched; but if you think you have some that you think are priority ones, we can could make an effort to try to get those first.

DR. SAMET: Karen.

MS. DeLEEUW: Along the lines of what both Ursula and Dorothy had mentioned, I know the states have quit lines, and there is a robust data set there. I don't know whether menthol or nonmenthol is asked, but I suspect there may be some states who have ventured into that. Perhaps contacting NAC, and seeing if they have any information about that.

Then, again, getting back to our charge we are also being asked to consider the potential for unintended public health consequences of banning menthol. I think that should be something that we

would also want to think about, and, perhaps, not just the public health effects.

DR. SAMET: Okay. I think we have two more questions. What I would like to do, since we're very close to running out of time, have five minutes for number three; five minutes for number four; five minutes to come back and talk about specific examples to tag on to our request.

So are there -- I think we have Jack and Greg, you have further things. Jack.

DR. HENNINGFIELD: Sure. In putting a call out for information that may help us out to NIH. I think is -- to be explicit, I think there potentially is a fair amount of information from NIH researchers. It may be that a request would have to go out that would provide some kind of resources or reimbursement or whatever to get those.

But I think something that's implicit, and I just want to make sure that others on the Panel agree with this; but what I am seeing is that the main likely source of public health harm is not necessarily that menthol makes the cigarettes --

make cigarette smoke more toxic or more additive, but rather the public health harm would be more in increasing initiation, perpetuations, decreasing sensation. So if a call goes out, I think that's really what we're looking for, unless others disagree.

DR. SAMET: As a priority, I mean, clearly found that information is available. Okay. Greg.

DR. CONNOLLY: Yes. I think it's a very, very important issue. I know we are under enormous time constraints. I think we can't take it lightly. I think every question we ask is very important to the health of America.

I would say any question we ask in the industry we should look in the internal documents, and just not USCF; NCI has funded a number of researchers that are experts over ten years now, looking at documents. Maybe it's separating out different questions and looking at contracting out, so the work does get done before this study is over.

I am really adverse to limiting the amount of information we have to make a decision. The

decision we make is going to bear upon every individual in this room, and every -- and the public health of this nation.

I think that general comments applies to dealing with issues of OMB clearance. I think we're in a very unfortunate position, but every question that we ask industry, I think, should be clearly looked at by experts who researched the documents. There is more than just USCF up here. There are other vendors. And I'm not including our entity in any way, shape, or form; but there are other expert groups that could be --

DR. SAMET: So let's move to -- do we really still have two more that want to speak to number two, or can we go on to three and four?

Dan first; quick.

DR. HECK: Just a cautionary note about the document side, and I use it myself. The preMSA documents and the preFDA authority documents may be of historical interest only moving forward; and we don't want to be looking at the '60 and '70's things, and necessarily drawing conclusions about

current activities.

DR. SAMET: Okay. Karen.

MS. DeLEEUW: I am just wondering, given Dr. Henningfield's observation, if it would make sense, then, to look at the population data before we look at the other data.

DR. SAMET: Okay. So I'm moving us to number three. I think, actually, I have heard several items. Are there agenda items that should be included in future meetings pertaining to menthol? I think we actually have touched on several. One is models. Another would be, I think, targeted industry document reviews; and I think we would have -- presume we would have to develop exactly what we wanted -- or Corinne, perhaps, you can help here, whether if we suggested that you consider mechanisms by which you could obtain document reviews related to at least the broad topics that we have set -- set out.

I understand that there is millions of documents, and we don't need to go all the way back to spud or whatever. But would you have enough

guidance from our discussion now? Because we're not going to refine this much in the next minute or two.

DR. HUSTEN: I think the main refinement we need are what are the exact questions that you want us to ask them to search? I mean, you have the list of 16, if those are the questions; but that's how they will get asked. So if you don't think those are the right questions, we just need to hear that.

DR. SAMET: We think they're the right major topics. I think we should probably be comfortable with those as a starting point.

So what else would we like to have as agenda items? And clearly this is not our last moment to define agenda items for future meetings. I think there are things we know we are going to want, and let's raise them now. We talked about additional analyses of data by CDC, for example, that's available.

We talked about what might be forthcoming from the epidemiological studies. Many of our things under our wish list under number two will

become items under number three; but other things to add. Greg.

DR. CONNOLLY: I think on June 22nd of this year that we ban the terms "light" descriptors in cigarettes. Some of those light products will be mentholated. So I would be very curious what impact the ban on light cigarettes have on the other descriptors for menthol. So examining the impact of the light descriptive ban on menthol cigarettes on both descriptors and possibly sales -- even sales.

DR. SAMET: I guess the issue there is whether data would appear in sufficiently a timely fashion for our report. It may not. It may be an example of the kind of surveillance activities that would be needed.

DR. CONNOLLY: I mean, I think there are, again, commercial data sets that FDA should make -- you know, should make available; you know, should explore. Nielsen, Simmons. Those are data sets. Maybe the turn around time is three months, but that's -- you know, that, to me, would allow us to complete the year. The more information we have to

answer this question in a scientific manner, the more we protect the public health.

DR. SAMET: Okay. Patricia.

DR. NEZ HENDERSON: This was briefly discussed this morning, is the impact that this policy, if it does go through, will have on cessation. So maybe doing some type of analyses on what's going to happen to African American smokers after the ban.

DR. SAMET: Yes, I, actually, think if we had the right models and they were subgroup specific, in fact, we would have, at least, some understanding of that. I think we have got that under models. Maybe make specific that we would definitely want those to extend to certain subgroups of interest. Mark.

DR. CLANTON: Well, assuming we haven't exhausted either a review or discussion of public health effects of menthol and tobacco -- or in tobacco, we probably need a placeholder on future agendas to make sure we're addressing public health impact. I know it's a general offering; it is not

specific. We probably need to make sure that we are addressing whatever current data or recent data is available on public health impact of menthol. That way just having that placeholder to make sure we do that. That's my suggestion.

DR. SAMET: Seeing nobody else wanting to speak to item three, we will move to four. I think my answer is a lot. But I think if we could -- I think it maybe not -- I'm not sure I see some highly specific answers coming out. I mean, clearly, we need literature review capability. You know, the ability to pull together systematic reviews on particular topics. Then, as we begin to write, I think we will have to discuss interactions around editorial processes, reference management. I think it would be great, for example, if we had the right web site portal with documents available. I don't know what's possible, or not possible.

I think if we could develop a substantial wish list for those who want to extend it, let's do so right now. Greg.

DR. CONNOLLY: I think I addressed this

maybe two days ago, and that is expertise within the Agency itself. There is expertise outside the Agency on issues of flavor, chemoperception. University of San Diego is one unit that studies chemosensory perception; Monell Institute, although there may be conflict of interest with Monell; flavor chemists who research flavor chemistry for the food industry and look at chemosensory perception; David Kessler recent book," "The End of Obesity" -- David is not with us today, but I think that's why we're here, in part -- provides a number of experts who understand the relationship between chemosensory perception and effects. I think the Agency would be wise to look at retaining consultants who could help with the report in the area of chemosensory perception from those different groups.

DR. SAMET: Let me ask a general question. Maybe, Corinne, you are about to respond. That is, if the Committee, itself, sees that it needs consultants in a particular area as opposed to let's say, FDA, what are our paths to do so?

DR. HUSTEN: Yes. You can give us names of folks that you like as consultants. We have several options. One would be we could ask them to come and present. Second, we could ask them to become consultants, which means they become SGEs, which is a process that takes a certain amount of time; and there is a certain amount of screening for conflict of interest that would ensue.

I would just say, you know, send us names of people that you think would be important, and we can explore what our options are with them.

As long as I have the microphone, I would also say if there are other publications that people feel we did not include or did not find in our search of the published literature, you could individually send us those references; and we would be happy to, you know, look at them and make sure that they're included.

So you could just send those individually. That doesn't break any kind of confidentiality problems, or you know, FACA problems.

DR. SAMET: As new publications come in

between meetings, how would you be providing them to us.

DR. HUSTEN: Well, generally, what we do is provide you materials before each meeting. So I anticipate we will be putting a system in place, you know, to keep updating the literature. Then we can provide that as part of the background materials for each of the meetings.

DR. SAMET: I will say I don't know how others feel, but it would be useful, I think, if important documents came in next we can, a we can from now -- you find this material that John mentioned, for example. I guess I would say it would be better for me to receive it not as part of a stack, but, you know, as such becomes available if it's possible to do so. I assume that would be the wish of others as well.

DR. HUSTEN: I will have to check into what we can and can't do.

DR. SAMET: Okay. Jack.

DR. HENNINGFIELD: Presumably, the Agency staff themselves through this process are getting a

better idea of what the universe is and what the options could be in terms of reports; but I think it would be helpful to think about what would minimally satisfy the requirements for a report; and to make sure we do that as opposed to everything that could be done.

And I mean, we have discussed what could be a four year Surgeon General's report. I mentioned on the other extreme, a two page World Health Organization recommendation. There are a lot of models for expert's reports that are published in the "New England Journal of Medicine," "Tobacco Control" that, you know, you could reference, have appendices. But I think getting a better idea of what would be satisfactory, that would incorporate ultimately questions, presumably, that you will come back to us with, that there may be a vote on for specific --

DR. HUSTEN: For this particular topic, I refer you back to the statute, and what the statute requires you to do and the provisions that it's asking you to take into consideration.

DR. SAMET: Mark.

DR. CLANTON: For this discussion I will assume that support and resources are sort of synonymous. So on the issue of references, I do admit that we have experts around the table who have probably read every primary source. But for those who haven't been able to do that, it would certainly be nice to have access to articles.

Now, I do understand there is already an issue -- technical issue about getting PDF versions of studies and reports, and whether they can be distributed or not. So I understand that may be a technical issue; but as a general matter if we can get access to primary sources, that would be good.

DR. HUSTEN: Again, we will try to get you everything within, you know, any constraints that we have. We also -- I think people referenced it, but just to make clear that in addition to the presentations, we are developing written summaries of the literature reviews that were done. So we can incorporate any other information that's sent to us. So you will also have that document as, you know,

something to refer back to; and we will figure out, you know, what we can do in terms of getting you all the references.

DR. SAMET: Okay. So what we're going to do now is we're going to go back up; and if we have examples of studies to insert into our list, let's do so now. So if we could go back up to the top.

So if you have something to insert, I think these probably don't need examples, but let's keep going down. I think we -- continue, I think, down. So here, for example, number seven.

So Jack, if you were going to add a "for example."

DR. HENNINGFIELD: Here I think we're looking for dose-response studies of behavioral, physiological, of which there are examples in the literature in drug abuse liability assessment, for example. But I think it's -- the danger of being too specific in the examples is the industry may have been using different models; and some of these data may have been collected decades ago, which then led to the setting of menthol levels that are used

today.

DR. SAMET: Okay. This one -- we probably should remove "abuse of liability," I think. I don't think we mean that. So let's -- so no example.

Let's continue down. Number eight, example to add anyone? Thumb down through that. Consumer perception study data.

DR. CONNOLLY: Well, you could -- focus group testing, research, quantitative panel testing research.

DR. SAMET: Okay. Why don't we just add those two.

DR. CONNOLLY: I would defer to Melanie on that, though.

DR. SAMET: Okay.

DR. WAKEFIELD: Yeah, I mean, they're just two examples; but I think -- I don't think we want to be limiting.

DR. SAMET: No. This is only to be exemplifying.

Biomarker studies, I think we are okay.

Marketing data here.

Consumer perception studies; anything you want to put there?

DR. CONNOLLY: Well, on the marketing data, I think commercial data sources would be of interest, such as Nielsen; there is Simmons data on this issue. I know some companies will retain outside firms to, you know, look at brand share and sales; and that data would be, you know, important commercial sources, as well as contracted sources. To the extent they rely upon those data sources -- they have data sources they are relying on that they may contract out.

Maybe it would be too limiting by --

DR. SAMET: These are intended only to be examples, remember that. Mark.

DR. CLANTON: I think a little further up Neal introduce this -- the idea of looking at studies, trying to understand metabolism, how menthol interacts, I guess, with nicotine metabolism -- it's up here somewhere. I just wanted to make sure if there were any specific examples you

wanted to offer that we didn't skip by that.

DR. BENOWITZ: I have not heard of any industry study about that. If there are studies, that's fine. I have not heard or seen of any.

DR. SAMET: Okay. Then, probably we need to hear from -- Corinne, let me just ask before we turn to her, if there is anything else.

We have remarkably gotten through questions one through four. I think we have written, what I hope are sufficiently cogent and specific items under question one. I don't think we're going to do better in the next 40 seconds. So please don't let us look at them anymore. And I think I will turn to, Corinne. Thanks.

DR. HUSTEN: Pulling up the slide here -- is this working?

Okay. Wanted to just let you know of some potential upcoming topics that we may be bringing before you. You know -- as you know, there is a statute in the provision that says that other topics can be brought to the Committee whether it's safety, dependence, or health issues related to tobacco

products.

So one possible topic that we are considering bringing before you is the topic of harmful or potentially harmful constituents. Some of the types of issues related to this topic include, the criteria for selection of the constituents, what the proposed list of harmful or potentially harmful constituents might consist of; qualitative rationale for including each constituent; acceptable analytical methods for assessing the quantity of each constituent; other ancillary standards, such as storage, or detection limits, or how the sample should be collected or processed; and the denominator for reporting the quantities is of the various constituents.

So just wanted to give you a head's up. Okay. The place, obviously, where notification of things occurs is through the Federal Register Notice, because when we are bringing topics before the Committee, that's how we post our proposed topics, and the questions that we would like answered at any meeting around those topics.

So just want to give you a heads up. We had heard during one of the discussions the suggestion that we bring topics before you. So we wanted to let you know that we are thinking about bringing other topics before you.

DR. SAMET: Greg.

DR. CONNOLLY: You know, and according to the statute too, we are required to bring advice to you. And I know what you presented is important. This is a comprehensive statute. It requires -- you know, it involves many, many activities that I think we have an obligation under the statute to bring advice to the FDA, just not listen. I think the upcoming -- well, just to mention the ban on flavors occurred. I would be very interested in being updated on what impact that has.

I just recently went to a web site of one of the manufacturers. I still see the listing of vanilla, cocoa, and licorice. I assume that's not characterizing. That just races a question. There is an upcoming ban on lights. To my knowledge, 73 countries have banned the terms "lights," yet, we

see no difference in sales. I would be very interested and concerned about what impact that congressional action is going to have on the consumption of lights in the United States of America.

There is interesting sections of the law. There is one section that, I think, the House considered, and that's the industry reporting unintended consequences of use of their product, as we do with drug manufacturers. I would be curious if the FDA is going to be looking at that particular provision.

So -- and this goes to Mark's point on placeholder. I think as a Committee to function and to fulfill the mandates of the law, we need a placeholder where we discuss broader issues, and discuss the comprehensive impact of this law on the health of America. And I am dedicated to assisting, advising, and helping in anything before us. I do feel an obligation as a member and reading the statute to also advise the FDA.

DR. SAMET: I actually think I might frame

a question out of this for you, Corinne, which would be -- for example, at a next meeting, which will, obviously, be focused on menthol, is there an opportunity for an updating of center activities generally? Let us know what's going on. In other words, can we have sort of a session in which there may be a general interchange as opposed to a particular constituent of menthol, or some other prespecified topic?

I mean, I do think it's useful, since you are in evolution and we are in evolution to hear from you about what is going on; and is there some -- an opportunity for my directional exchange in such a forum as Greg is suggesting that would be useful?

DR. HUSTEN: I believe we do have the ability to give you an update on, you know, what's happened since the previous meeting.

DR. CONNOLLY: Just one point to Corinne. I did mention it. I know the issue of warning labels are coming up. I was just thinking last night, this law is really intended to help smokers.

I think that's our obligation. I have seen other countries look at the issue of, you know, warning labels. I just question if they're showing respect and dignity to smokers in America.

I hope everything we do shows respect and dignity to smokers in any area. That may not be a scientific statement, but I think the basis of science is based on basic philosophical concepts, which goes back to human rights, and respect and dignity. I just hope -- and it's maybe a philosophical statement that everything we do we respect the dignity of smokers, and we help smokers. We're here to help smokers. I think it's very, very important. I just want to stress that as a member.

DR. HUSTEN: I don't think anyone at FDA would disagree with you.

DR. SAMET: Okay. Are there other comments? We can finish five minutes early. John.

DR. LAUTERBACH: You know, we had on the agenda here as a topic three -- this -- I guess these things about the harmful constituents. Is that essentially postponed now to a second meeting?

DR. SAMET: I think that was only a preview of things that might be coming. So that's not for topic. So with Patricia.

DR. NEZ HENDERSON: I just wanted to find out that as we move forward on this legislation that we really consider native tribes, and -- in the discussion, because they're sovereign communities. And when the legislation was passed last June, you know, they're now charged with enforcement. I think it really needs to be considered as we move forward.

DR. HUSTEN: And that is an area that we're actively working on.

DR. SAMET: Okay. Thank you. I think what we're going to do is move to closing remarks from Dr. Deyton, the center director. You might notice that while you were allocated a half hour, there is five minutes left.

DR. DEYTON: I accept a friendly amendment from the Chair. I will just sit here and make a couple of comments.

First, back to really where I started the other morning. I want to thank all of you for --

for agreeing to do this. When I said it yesterday morning, I think that it was a notional thank you. Now, you understand some of the complexities that we're all going to be dealing with for many years to come. So your -- the spirit with which all of you are coming to the table, the openness, being able to talk to each other, think out loud, work together as a group is very important to us in FDA. We really do want to thank you for that.

I want to take just a moment and thank a couple of people who have pulled this together. Obviously, your acting DFO.

Cristi, you have done a phenomenal job in getting us here. Thank you for all of that.

Corinne has been helping us all prepare for the scientific issues, which we're talking here; and thank you for your leadership here. Certainly, the presenters that we heard from yesterday, I think, did a masterful job at synthesizing a lot of information. Certainly, not all of it yet, but we were trying to give this Committee a bit of a jump, a bit of a head start.

So thank you for -- to those presenters, all of you who participated in that. And thank all of you for listening to their -- their work and their comments in the spirit with which they're given.

Karen, our pillar back here; Tom Graham, as well. A lot of people to thank to put this on. We will all get to know each other a lot better as the years go forward. If you have suggestions for how these meetings can help you do your work for us, please don't hesitate, let Cristi know. We want to make these meetings -- deliver for you the best environment for you to give FDA the advice that we need you to give us.

I think this was a really phenomenal start of what, obviously, is going to be a lot of activity over the years. I think in terms of the topic that we have talked about today, menthol, I appreciate all of you being very cognizant of the statutory deadlines that this Committee is under to give us that FDA advice.

Please, take all of the information that

we're going to now go out and try and pull together for you. We will keep you as informed about what we can and cannot do as we possibly can, and look forward to seeing all of you again soon. Thanks very much.

And Jon, thank you for your leadership as Chair. Truly wonderful.

DR. SAMET: Thanks. Thank you all; and there may be days when you are not clapping at the end of the day.

So thanks, everybody, for the hard work, to the FDA, our public presenters. And see you all when we see you next. Yeah, good travel back home.

(Whereupon, at 2:58 p.m., the proceedings were adjourned.)

CERTIFICATE OF REPORTER

I, Stella R. Christian, A Certified Shorthand Reporter, do hereby certify that I was authorized to and did report in stenotype notes the foregoing proceedings, and that thereafter my stenotype notes were reduced to typewriting under my supervision.

I further certify that the transcript of proceedings contains a true and correct transcript of my stenotype notes taken therein to the best of my ability and knowledge.

SIGNED this 16th day of April, 2010.

_____
STELLA R. CHRISTIAN